The Journal of the American Medical Association

Published Under the Auspices of the Board of Trustees

VOL. 134, No. 12 — CHICAGO, ILLINOIS — JULY 19, 1947

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DIAGNOSIS OF MYASTHENIA GRAVIS IN PATIENTS WITH DYSPHAGIA

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Dysphagia is one of the commonest symptoms of myasthenia gravis. Moreover, it may often be the presenting symptom, some difficulty in swallowing being the first sign of abnormal muscular fatigue. The defect in the swallowing reflex is due to weakness of the buccopharyngeal muscles, usually with relaxation of the constrictors. Both the feeble power of the reflex act, as shown by the slowness of movement, and the relaxation, with dilation of the pharyngeal tube, are easily demonstrated by roentgenoscopic examination. The tightening of these muscles and the increased rate of swallowing, after stimulation by an appropriate amount of neostigmine ("prostigmine") methylsulfate, was observed and recorded in cases of myasthenia gravis by Schwab and Viets [1] in 1941. They suggested that this method of examination might be used as a test for the disease, and the present communication is in effect a reinforcement of the observations of 1941 in the light of five more years of experience.

DYSPHAGIA AND DYSARTHRIA IN MYASTHENIA GRAVIS

In the last eleven years, 175 cases of myasthenia gravis have been studied at the Massachusetts General Hospital. An analysis of this entire group indicates that dysphagia and dysarthria occur at the onset as the first symptom in about 20 per cent of the patients. Thirty-five of the 175 patients had one or both of these symptoms (fig. 1). Dysphagia is commoner than dysarthria, although usually the two occur together. The dysarthria, indicated by nasal speech, seldom occurs alone and is to be considered as a minor symptom. The defect is in the soft palate, not in the vocal cords. Dysphagia, on the other hand, often may be present without any dysarthria.

In addition to being the first symptom in myasthenia gravis, dysphagia may occur in the course of the disease, at which time it is usually indicative of an exacerbation. Dysphagia is one of the more important symptoms, moreover, from the point of view of prognosis. When present the patient may lose weight rapidly and be subjected to choking or coughing spells. As a symptom, therefore, dysphagia is of more importance, except for dyspnea, than, for instance, ptosis and diplopia or general muscular weakness.

The first symptoms of myasthenia gravis occur at all ages, but the disease begins most frequently between the ages of 20 and 30 (fig. 2). Fifty-two of the 175 cases studied began during this decade. It is also relatively frequent between 60 and 70 years of age. From the point of view of the laryngologist, this later period becomes of considerable importance, for between ages 60 and 70 is the period when other forms of dysphagia, particularly those due to intrinsic degenerative diseases of the central nervous system and obstruction caused by tumor formation, are commonest. Bulbar palsy occurs at this age of life.

Myasthenia gravis, moreover, may occur in patients over 70, and I have had 10 such instances. In the younger age groups, 4 have occurred before the age of 10 and 26 between 10 and 20 years of age. There is a scattering of cases between 30 and 60 years, and no decade of life is free from examples of the onset of this disease, save possibly the ninth.

Of all the symptoms, ptosis and diplopia are the commonest, occurring in 43.4 per cent of the 175 patients who were examined. Next in frequency is general weakness due to involvement of the arms and legs. This was found in 34.2 per cent. Weakness of the muscles of the neck occurs in 2.3 per cent. Dysphagia and dysarthria account for the remaining 20.1 per cent (fig. 1).

The disease, formerly considered fatal in a large percentage of cases, is now considerably controlled by the use of neostigmine either given orally or by injection. In this series, 35 patients have died in the course of eleven years, a mortality of 20 per cent. Before the use of neostigmine the death rate, over a similar period, would have been about 75 per cent.

The progress of the disease offers great variability. The symptoms of some patients are fixed for long periods of time. On the other hand, there is not infrequently a tendency toward progress by remissions and relapses. Thirty-one per cent of the patients have shown some tendency toward remission, and 14 per cent of the patients have had complete remissions during the period of observation. Spontaneous remissions may occur, no matter how severe the symptoms of the patients may be during the height of their relapse.

The symptoms of myasthenia gravis are entirely due to weakness of the muscular action. Except for the act of swallowing, the muscles involved are those concerned with voluntary movements. The muscle dysfunction is due to fatigue, with normal action usually possible after a period of rest. There are indications that the abnormal fatigue is caused by a chemical disturbance in the acteylcholine-cholinesterase balance

From the Myasthenia Gravis Clinic, Massachusetts General Hospital.
Read before the Section on Laryngology, Otology and Rhinology at the Ninety-Fifth Annual Session of the American Medical Association, San Francisco, July 3, 1946.

1. Schwab, R. S., and Viets, H. R.: Roentgenography of the Pharynx in Myasthenia Gravis Before and After Prostigmine Injection, Am. J. Roentgenol. 45:337 (March) 1941.

at the myoneural junction or possibly in the muscle itself. Whatever the mechanism giving rise to the symptoms, it is now accepted that neostigmine has an unusual effect in overcoming the excessive fatigue of muscular motion. When the drug is taken, either by mouth or parenterally, the response is often prompt

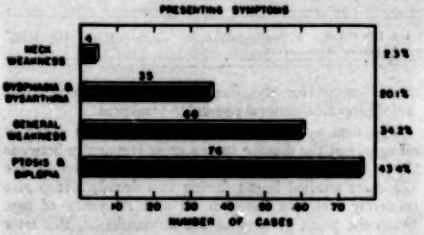

Fig. 1.—The first symptoms of myasthenia gravis in a group of 175 cases. Some defect in swallowing or speaking occurs in one-fifth of the cases.

and may be complete. As the effect of neostigmine on other diseases is either slight or nil, the drug is useful as a diagnostic agent.

THE NEOSTIGMINE TEST

The neostigmine test may be carried out as an office procedure, but if the patient is seriously ill, the test is usually performed in the hospital. If the patient has not been taking neostigmine in any form and appears for diagnosis because of dysphagia, care should be taken in doing the test for two specific reasons. First, patients not suffering from myasthenia gravis may have a general reaction to the neostigmine and second, patients with bulbar palsy or other conditions giving rise to permanent muscular weakness may find it difficult to swallow the barium paste without choking.

For an adult, 1.5 mg. of neostigmine methylsulfate and 0.6 mg. of atropine sulfate are combined in a 1 cc. ampule, known as the diagnostic ampule. This special form of neostigmine should not be confused with the ordinary treatment ampule of neostigmine methylsulfate, 1 cc. of which contains 0.5 mg. of a 1:2,000 solution. Experience has shown that the amount of neostigmine in the diagnostic ampule is necessary in order to obtain a satisfactory test in an adult. The atropine is added to overcome the stimulation of the parasympathetic system. Ampules of atropine sulfate should be at hand to inject promptly provided the patient shows symptoms of severe parasympathetic stimulation, such as intestinal cramps, diarrhea, cold sweats or collapse. Most patients with myasthenia gravis are relatively free from reactions of this type. No patient is known to have died as the result of an injection of neostigmine as a diagnostic test, but the results may be disturbing to a roentgenologist who is not prepared to handle the situation. A violent reaction to neostigmine is almost certain evidence that myasthenia gravis is not the correct diagnosis.

If the barium paste is thick the patient may have considerable difficulty in swallowing it, particularly if suffering from permanent paralysis such as occurs in bulbar palsy. A thinner mixture should be used under these circumstances.

If the patient is taking neostigmine, the dosage of the drug should be omitted for at least twelve hours before the test is performed. In severe cases, only partial omission of the medicament may be possible. The examination is then made in the usual manner by observing the patient, ordinarily in the upright position, under the fluoroscope as the barium paste is swallowed. If the barium is retained in the pharynx a plate may be taken, thus recording the amount of retention. After the preliminary studies have been made, the patient is given a subcutaneous injection of the contents of the diagnostic ampule. In twenty to thirty minutes, reexamination is made following the same procedure.

ILLUSTRATIVE CASES

In most cases of myasthenia gravis, patients with dysphagia as the presenting symptom will respond to the neostigmine test completely. However, in mild cases the retention of barium in the pharynx before injection may not be pronounced, particularly if a thin solution of barium paste is used. After the injection the barium is completely removed, except for a minimum amount often left in the pyriform sinuses. This should be evacuated in the average patient after the second and third swallowing. In most cases there is no retention. No other disease except myasthenia gravis gives rise to such a complete return of normal function of the swallowing reflex after the appropriate amount of neostigmine is given and the patient is allowed to absorb the medicine over a period of twenty to thirty minutes. An example of this type of reaction which would be considered a positive neostigmine test, completely diagnostic of myasthenia gravis, is given in the following case history:

Case 1.—*History.*—H. R., a man aged 34, first noticed generalized muscular weakness with difficulty in chewing and swallowing in March, 1942. On examination two weeks after the onset there was ptosis of one eyelid, diplopia and inability to wrinkle the eyebrows or to close the eyes tightly. When his arms were extended in front of him they dropped in a few seconds. He fell when attempting to walk up some stairs. Because of the weakness of the muscles of the neck, he had

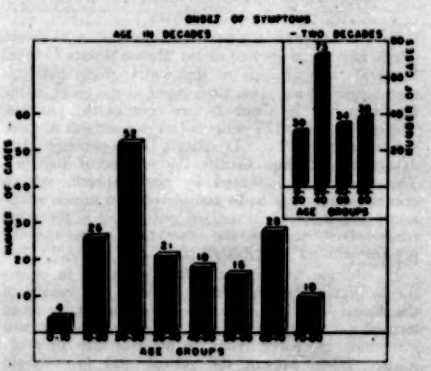

Fig. 2.—The age of onset in 175 cases of myasthenia gravis, by decades and double decades. Over 40 per cent of the group had their first symptoms between 20 and 40 years of age, but the disease began in all decades.

difficulty in holding up his head. The act of swallowing was slow and labored, but there was no regurgitation of fluids through his nose. His jaw tended to hang half open, and his speech was slurred.

Roentgen Examination (March 19, 1942).—A swallow of barium was given and roentgen examination showed slight filling

of the pyriform sinuses with little delay in the passage of the barium through the pharynx and upper esophagus (fig. 3 *A*). After injection of the neostigmine, the swallow was repeated and showed rapid passage of barium, with no filling of the pyriform sinus (fig. 3 *B*). Examination of the swallow of barium before and after the injection of neostigmine showed definite changes in the muscular movements of deglutition.

Subsequent Clinical Course.—The patient responded well to neostigmine bromide taken at appropriate intervals by mouth. A thymectomy was performed April 21, 1943, and a benign thymoma was removed. The condition of the patient improved slightly immediately after operative intervention, but he subsequently had increasing symptoms and died of respiratory paralysis Oct. 15, 1944, about a year and a half after the operation. There was no thymic tissue present at autopsy.

In severer cases the response to the diagnostic ampule of neostigmine may not be so complete. Two of the ampules may be used, but usually one is sufficient. The roentgenologist should guard against making a mistaken report of "no improvement" when insufficient neostigmine has been employed. It is always better to repeat the test with an increased amount of neostigmine, if there is reasonable doubt in the mind of the examiner, and not accept an inconclusive result. If the barium paste is moderately thick no harm should come to the patient by repeating the test even at the same sitting.

Fig. 3 (case 1).—*A*, appearance of the pharynx, showing slight retention of barium before injection of a diagnostic ampule of neostigmine methylsulfate; *B*, appearance of the pharynx after the injection of a diagnostic ampule.

CASE 2.—*History.*—J. K., a woman aged 29, had experienced difficulty in swallowing and talking for about a month before being seen in December 1943. She had also noticed about the same time some intermittent weakness of the little fingers. On examination, she was unable to swallow any solid food and could swallow only a slight amount of liquid, without fatigue or regurgitation. Her voice was nasal in type to a sufficient degree that her speech was difficult to understand. Saliva tended to accumulate in her mouth. Ptosis of the left eyelid was present but no diplopia. Some weakness of her legs was noticed in climbing stairs.

Roentgen Examination (Dec. 30, 1943).—Before the injection of neostigmine roentgen examination showed decided retention of barium in the valleculae and pyriform sinuses (fig. 4 *A*). There was considerable difficulty in swallowing. The hypopharynx ballooned out considerably. After administration of neostigmine methylsulfate, the swallowing act was greatly improved and the tonus of the hypopharynx approached that of a normal person (fig. 4 *B*).

Subsequent Clinical Course.—The patient has been maintained reasonably well on a regimen of neostigmine bromide by mouth, supplemented with some injections of neostigmine methylsulfate, particularly before her meals. It was necessary for her to be hospitalized in 1945 in order to adjust her medical regimen. When she was properly maintained on an adequate dosage of neostigmine, the patient gained 10 pounds (4.5 Kg.) in a few weeks.

Occasionally, the improvement after injection may be insufficient to make a report of a positive test. Although the retention may be considerable, the increased rate of the swallowing reflex, as noted under the fluoroscope, is usually the most dependable observation. Much of the barium, moreover, may be

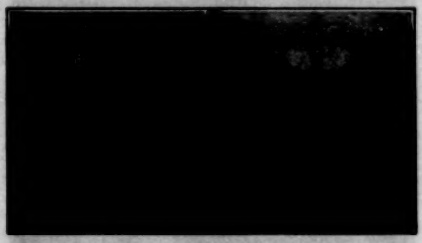

Fig. 4 (case 2).—*A*, anterior posterior view of the pharynx, showing the accumulation of barium in the valleculae and pyriform sinuses; *B*, appearance of the pharynx about twenty minutes after injection of the diagnostic ampule.

removed on a second or third attempt to swallow, often an impossible act prior to the administration of neostigmine. A normal swallowing reflex, in spite of considerable retention of the barium, is illustrated by the following case:

CASE 3.—*History.*—B. C., a man aged 60, had increasing difficulty in swallowing for a period of two months prior to being first seen, Sept. 2, 1943. During this period he had lost 25 pounds (11 Kg.), and about six weeks before entering the hospital he had given up his position as a grocery clerk. He had no regurgitation of liquids through his nose, and he had not vomited. In addition to the difficulty in swallowing the patient had noticed bilateral ptosis of his eyelids and his speech had become nasal in character. There was an increasing tendency for secretions to accumulate in his mouth and pharynx. There also developed a slight weakness in his right leg with a tendency toward foot drop. On examination, there was bilateral ptosis, his speech was nasal in character and chewing and swallowing of solid foods was impossible. He could ingest a slight amount of liquid. The jaw sagged, and there was considerable weakness in the facial muscles, particularly around the mouth. Diplopia was not present.

Fig. 5 (case 3).—*A*, retention of barium in the pharynx in a patient with well defined dysphagia due to myasthenia gravis. *B*, effect of the injection of a diagnostic ampule, showing partial improvement in the swallowing reflex.

Roentgen Examination (Sept. 15, 1943.)—A large amount of barium was retained in the pharynx prior to an injection of a diagnostic ampule of neostigmine (fig. 5 *A*). Most of this disappeared twenty minutes after the injection, and the patient's swallowing reflex became relatively normal (fig. 5 *B*).

Subsequent Clinical Course.—The patient was maintained on large amounts of neostigmine bromide by mouth, supplemented

by injections of neostigmine methylsulfate before the noon and evening meal. He learned to give the injections himself. Slow but steady improvement was noticed, and within a period of a month he was able to omit one injection a day, keeping his oral medication at a level of twelve tablets in twenty-four hours. He gained 10 pounds (4.5 Kg.) in two months, and at the end of three months was able to give up the injections entirely and gradually reduce the amount of medicine by mouth. Six months after the onset the patient was in a state of complete remission, having no symptoms and not needing any medicine either by mouth or injection. He was able to undergo a minor surgical operation at the end of one year and has remained well for a period of slightly over two years.

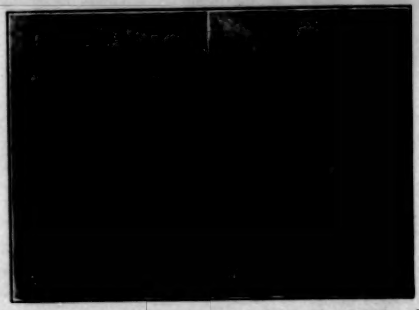

Fig. 6 (case 4).—*A*, normal swallowing reflex without retention of barium, in patient well maintained on oral neostigmine. *B*, patient without oral neostigmine for thirteen hours, showing defective swallowing reflex with retention of barium.

The test may be used as a check of the efficiency of treatment in patients with myasthenia gravis who are being maintained on oral neostigmine. Ordinarily this is not necessary or even desirable, but occasionally one may wish to find out whether the swallowing reflex is still affected even though the patient is free from symptoms. By omitting the oral medication for twelve to twenty-four hours, the test can be done exactly as it is performed as a diagnostic measure. In the following case this was the method used:

Fig. 7 (case 5).—Pronounced retention of barium, just prior to a spontaneous remission, with complete recovery in four months.

Case 4.—*History.*—M. S., a woman aged 30, began to have dysphagia about three years before her admission to the hospital in February 1943. Subsequently she noted the development of ptosis, diplopia, dysarthria and some general weakness. She was quickly adjusted to a schedule of oral neostigmine. Under treatment she was free from symptoms. Her scheduled intake of medicine was omitted for thirteen hours, as a test of its efficiency. At the end of the period the patient had pronounced difficulty in swallowing and her speech was nasal in character.

Roentgen Examination (Feb. 4, 1943).—While the patient was well adjusted on oral medication, she was given a swallow of barium and roentgen examination showed no delay in the passage of the barium and no filling of the pyriform sinuses (fig. 6 *A*).

Reexamination of the patient who had not taken medicine for thirteen hours showed pronounced difficulty in swallowing. The patient choked during the examination and retained barium in the pyriform sinuses (fig. 6 *B*). Twenty minutes after injection with neostigmine the patient again swallowed in a normal manner and barium was not retained.

Subsequent Clinical Course.—After she left the hospital, the patient was well maintained on oral neostigmine for about two years. She then relapsed and died of respiratory paralysis in another hospital on Aug. 24, 1945.

Although dysphagia may be decided and the patient may show other serious signs of myasthenia gravis, recovery may be rapid soon after the diagnosis is made. The dysphagia, with pronounced retention of barium, may disappear completely in a few months. An example of such a spontaneous remission is as follows:

Case 5.—*History.*—C. Y., a woman aged 72, began to have dysphagia six months before entering the hospital on July 18, 1945. Prior to the actual onset, she had noticed intermittent weakness of her pharynx and slight difficulty in swallowing of a transient character for a period of nearly five years. The last part of her meal was often difficult to ingest, but her symptoms did not become decided until December 1944. Solid food tended to be retained in her pharynx, and when she attempted to wash it down with fluids, the fluid would be regurgitated through her nose. She never had dysarthria. In a year's time, she lost about 15 pounds (6.8 Kg.) in weight.

Fig. 8 (case 6).—*A*, decided retention of barium in the pharynx and pyriform sinuses in a case of myasthenia gravis with dysphagia. *B*, almost complete removal of barium from the pharynx, but with some retention in the pyriform sinuses, after injection with neostigmine in the diagnostic test.

On examination, the chief difficulty was in swallowing.

Roentgen Examination (July 18, 1945).—There was well defined paralysis of deglutition, and barium was retained in the pyriform sinuses and valleculae in large amounts (fig. 7). After a diagnostic test with neostigmine, the swallowing reflex was much improved.

Subsequent Clinical Course.—The patient rapidly advanced to a spontaneous remission of her symptoms. She only took a small amount of neostigmine for a few days. Her condition improved rapidly, however, and her tablets were soon omitted. At the end of about a month she was able to swallow in a normal manner. When seen in November 1945, four months after the testing, she showed no dysphagia and was not taking any medicine.

Not infrequently, the cases of patients suffering from dysphagia as the chief symptom are diagnosed as bulbar palsy. It is rare, however, to have bulbar palsy without atrophy and fibrillations easily observable in the tongue and posterior pharyngeal muscles. Moreover, in this disease the speech is commonly of the "hot potato" type and not the typical nasal speech heard in patients with myasthenia gravis. Patients with myasthenia gravis are unlikely to have dysphagia

as the only symptom if a careful history and examination are conducted. One usually finds weakness of the masseter muscles, transient diplopia and ptosis and some evidence of general muscular weakness. Patients, however, may go many months or even years with their disease undiagnosed. The diagnosis may be surprisingly easy when the patient's swallowing reflex is studied before and after an injection of neostigmine. This is illustrated in the following case:

CASE 6.—*History.*—H. G., a man aged 71, was first seen in March 1946. Ten months before examination he first noticed weakness of the muscles of his neck, and later, diplopia. Three months after the onset, there was weakness of the masseter muscles and it was necessary for him to hold up his chin with his hand. About the same time dysphagia and dysarthria developed. At times there was great difficulty in swallowing and fluids were regurgitated through his nose.

Roentgen Examination by Dr. A. S. MacMillan (March 28, 1946.)—Roentgen examination revealed decided stasis in the pharynx with retention of barium in the pyriform sinuses before the injection of neostigmine (fig. 8*A*). After the test the condition of the patient was greatly improved, although some retention was still evident (fig. 8*B*).

Subsequent Clinical Course.—The patient was adjusted on a schedule of oral neostigmine and improved quickly. Three months after the examination the patient was well maintained on oral medicaments and was almost free from symptoms.

Of the cases chosen to illustrate the diagnostic test it will be noted that 3 of the patients were over 60 years of age and 2 of them over 70. It is in this group, usually first seen by the laryngologist, that the diagnosis is most likely to be missed, for it is the age when degenerative or neoplastic disease is most frequent. The matter should be resolved by the neostigmine test. The test has never been found to be positive in any patients in whom there was reasonable doubt in regard to the diagnosis of myasthenia gravis, and seldom will the test be negative in this disease if the patient has dysphagia as one of the symptoms and is not fully adjusted on a regimen of oral medication.

CONCLUSION

1. If dysphagia is present as a symptom of myasthenia gravis, the response to neostigmine observed under the fluoroscope when the patient is seen in the act of swallowing provides a diagnostic test of considerable value.

2. In no other disease will swallowing be improved as the result of the test. In myasthenia gravis patients with dysphagia, provided they are not fully adjusted on oral neostigmine, will show a prompt and unequivocal response.

3. The amount of the drug to be used is provided in a diagnostic ampule which contains 1.5 mg. of neostigmine methylsulfate and 0.6 mg. of atropine sulfate. The injection is given subcutaneously, and observations are made twenty to thirty minutes later.

4. In a positive test the pyriform sinuses are usually emptied and there is no retention in the valleculae or along the walls of the pharynx. The tone of the pharyngeal muscles may be improved, as seen by increased constriction.

5. A medium thin barium paste should be used, not so thick as to be normally retained either by the pyriform sinuses or along the walls of the pharynx.

6. The response in patients not suffering from myasthenia gravis is nil. These patients, moreover, may have considerable general reaction to the neostigmine due to parasympathetic stimulation. In order to avoid this, atropine sulfate is added to the diagnostic ampule. Certain patients may be particularly sensitive to the neostigmine, and, if so, additional amounts of atropine sulfate should be available at the time of the test.

7. This test for dysphagia is part of the general neostigmine test for myasthenia gravis, but it is particularly valuable in making the diagnosis because of the absence of voluntary control and the clear method of observation by fluoroscopic examination.

ABSTRACT OF DISCUSSION

DR. HENRY W. NEWMAN, San Francisco: Dr. Viets has seen enough cases that he can determine the percentage that have various symptoms. He has stated that in approximately 20 per cent of the cases dysphagia may be the symptom with which the patient presents himself. In other manifestations of myasthenia it is frequently easy to determine by observation the part under stress of function. The myasthenic action of tiring out is quite apparent. Myographic studies can be made and the difficulty easily determined. When the difficulty is in swallowing, frequently there is a great deal of trouble in demonstrating this difficulty, except by the roentgenographic method. This is something which should be done in all patients in whom the diagnosis is not at once apparent. Dr. Viets stated that this enables one to differentiate between myasthenia and degenerative diseases of the nervous system, such as progressive bulbar palsy. The test is also of value in differentiating between various functional nervous complaints, such as hysteria, in which the patient frequently complains of difficulty in swallowing. "There is a ball in my throat which won't go down." This may be purely a hysterical symptom or it may be a presenting symptom of myasthenia gravis. If the person shows difficulty in the swallowing mechanism roentgenographically and this difficulty is cleared up with neostigmine, the physician knows he is not dealing with a neurosis but with myasthenia gravis. Dr. Viets has shown that these patients will get well or relatively well spontaneously or go into a remission which may last a matter of years. One must always bear this in mind in evaluating the reports which have been made in regard to removal of the thymus in this condition. Certainly, the fact that Dr. Viets and others have seen patients from whom presumably a thymoma was removed and who nevertheless have gone downhill in spite of all treatment and in whom at autopsy there has been no evidence of thymus remaining must definitely indicate that aberrant function of the thymus may be one factor in the production of myasthenia gravis. It is not by any means the only factor.

DR. VICTOR GOODHILL, Los Angeles: I should like to offer information which might be of help in the diagnosis. At the University of Southern California School of Medicine, in the Department of Anatomy, a method of motion picture roentgenography has been devised by Drs. Irving Rehman and Paul Patek. From the Department of Otolaryngology, I have been able to send them a number of patients with various difficulties in swallowing, including several patients with bulbar palsies, several patients with cancers of the hypopharynx and larynx and several tracheotomized patients. It is possible to take these motion pictures under the roentgen ray with barium swallows and to follow beautifully, with slow motion reproduction, the exact operation of the swallowing mechanism. I have seen rather startling demonstrations of palsies of the muscles of deglutition under the controlled guidance of a slow-motion picture roentgenographic reproduction.

DR. HENRY R. VIETS, Boston: There are two particular points that I should like to add. One is that the diagnosis of myasthenia gravis is easily made now by injection of the proper amount of neostigmine methylsulfate. This is put up in a special diagnostic ampule which contains the correct amount to use for an adult. If one uses too little, as in the ordinary treatment ampule, one will not get sufficient response, so that some cases will be incorrectly diagnosed on that account.

The second point I should like to make is that the drug neostigmine is an extremely powerful stimulant, particularly in a patient who does not have myasthenia gravis. A normal person taking neostigmine will experience, in some cases, a parasympathetic stimulation of such a degree that he may even collapse. It is on account of this parasympathetic stimulation which occurs in normal persons that atropine is added, and it is advisable to have additional injections of atropine available when this test is made, particularly if the person does not happen to have myasthenia gravis.

DIAGNOSIS OF ANEMIAS IN INFANCY AND CHILDHOOD

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New York

The diagnostic features of the anemias in infancy and childhood are influenced by numerous physiologic and anatomic changes which take place within and outside of the hematopoietic system. Alterations of the blood need to be interpreted, therefore, against the shifting background of normal hematologic changes which take place from birth through childhood. During this period the condition of the peripheral blood may reflect the results of the isoimmunization of the mother by fetal blood factors, abnormalities in maternal hematopoiesis, prematurity, the effect of rapid body growth, limitation of reserve bone marrow, reactivation of fetal blood sites and the greater inherent capacity of the hematopoietic system of younger subjects to react excessively to stimuli which would have little effect on an adult.

In this age period the anemias develop insidiously, and diagnosis before specific criteria are established may be difficult. Diagnosis is facilitated by the appraisal of data derived from various sources: history and physical examination, reference to age periods of most frequent incidence, comparison with the normal range of hematic values for each age period, study of the bone marrow by sternal aspiration, the roentgenogram, the hereditary aspects of the disease, careful scrutiny of the blood smear and the therapeutic response to liver, iron and folic acid.

In this presentation the criteria by which a specific disease is diagnosed will be discussed while elaborating more general considerations. Certain especially adapted technical procedures which have been found useful in establishing more precise quantitative data will be described.

HISTORY AND PHYSICAL EXAMINATION

Questions along the broad lines of causation will frequently reveal facts which lead to ready diagnosis. Information should be obtained concerning the onset of pallor, of purpura; the loss of blood from the bowel; infection, including exposure to animal parasites; the use of drugs known to affect hematopoiesis; renal disease; the rapidity of growth; overfeeding of milk with the refusal of solid foods, and the existence of anemia in the mother during pregnancy.

Information in regard to race and nationality is important in the diagnosis of sickle cell anemia and Mediterranean anemia. While sickling of the red blood cells occurs almost exclusively in the Negro race, it has been observed occasionally in the white families which are principally of Mediterranean origin. In Mediterranean anemia the patients are mainly of Greek, of Italian (principally Sicilian and from the Italian peninsula below Naples) or, less frequently, of Syrian origin. Lately a few authentic cases have been recognized among Chinese, Asiatic Indian, Turkish and Egyptian children, and recently Faber and Roth [1] described a case in a Negro girl. There is growing evidence that the trait and mild forms of Mediterranean anemia (familial erythroblastic anemia) occur with greater frequency in this country than published reports have indicated. Since the milder forms may occur in one or both parents born in this country, it is necessary to determine whether any of the grandparents are of Mediterranean origin.

While pallor is frequently misleading as an indication of the degree of anemia, its presence is a valuable diagnostic aid. The history of its onset as obtained from parents is occasionally vague and unsatisfactory, particularly in the chronic forms of anemia. In this connection Wintrobe [2] has pointed out that the physiologic adjustments in chronic anemia may be so efficient that physical activity can be carried out for long periods of time with decidedly lowered hemoglobin levels.

In advanced cases of Mediterranean anemia the skin and facies present a striking diagnostic appearance. The pale, muddy yellow pigmentation of the skin and mongoloid facies produced by changes in the skull bones are characteristic of the established form of Mediterranean anemia. In those instances of aplastic anemia in which the course is prolonged, the increasing pallor is in some instances replaced by a dark pigmentation of the skin which during terminal phases assumes an aspect of bronzing. The value of examination of the skin in diagnosis of anemia is exemplified by a careful history of the exact timing of the development of jaundice. The history of the earlier onset and increasing depth of jaundice in erythroblastosis fetalis differentiates it from the slowly progressing and milder degree of jaundice associated with icterus neonatorum. Visible jaundice at birth and its deepening for a few days is of diagnostic value in those cases of erythroblastosis fetalis in which there is no anemia and in which the number of nucleated blood cells is only slightly increased.

Splenomegaly is commonly found in infants and young children suffering from anemia due to a variety of causes. Enlargement is most noticeable in the diseases associated in some manner with hematic destruction, such as erythroblastosis fetalis, acute hemolytic anemia, familial hemolytic jaundice, sickle cell anemia and Mediterranean anemia. In this group it is not uncommon for an increase in the size of the spleen to occur during periods of pronounced anemia and for shrinking to follow during quiescence, particularly as a result of transfusions. In sickle cell anemia the spleen is most likely to be enlarged in infants and young children and to become progressively smaller and more fibrotic as the patient gets older. In patients with an active form of congenital hemolytic jaundice and in Mediterranean anemia the spleen is enlarged, at times to an excessive size. In patients with the mild

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Read in a symposium on "Anemia in Infancy and Childhood" before the Section on Pediatrics at the Ninety-Fifth Annual Session of the American Medical Association, San Francisco, July 3, 1946.

1. Faber, H. K., and Roth, B. M.: Mediterranean Anemia (Cooley) in a Negro Girl, J. Pediat. 28:610 (May) 1946.
2. Wintrobe, M. M.: The Cardiovascular System in Anemia with a Note on the Particular Abnormalities of Sickle Cell Anemia, Blood 1:121 (March) 1946.

form of both conditions the spleen is either not felt at all or is barely palpable. In young children with anemia of comparable severity the spleen is more likely to be enlarged in Mediterranean anemia than in sickle cell anemia or in congenital hemolytic jaundice. The spleen may be slightly enlarged in anemia due to iron deficiency and in megaloblastic anemia of infancy. It is not enlarged in aplastic or hypoplastic anemia or in the anemia of prematurity.

Except for the anemia associated with infection or with leukemia, lymphadenopathy is not a conspicuous clinical feature of the anemias. Enlarged cervical nodes frequently associated with palpable spleen occur in the anemia due to infection of the upper part of the respiratory passages. The superficial lymph nodes may be slightly enlarged in Mediterranean anemia but not in the other intrinsic anemias. A generalized enlargement of the lymph nodes in the presence of a refractory anemia should arouse suspicion of leukemia. In the early stages of leukemia with leukopenia when no blast cells appear in the peripheral blood the spleen and lymph nodes may not be appreciably enlarged. In these instances the cause of the anemia can be ascertained by the discovery of the blast cells in the bone marrow.

AGE INCIDENCE OF THE ANEMIAS IN RELATION TO DIAGNOSIS

When infection which is responsible for the major number of anemias in younger persons is excluded as an etiologic factor, the remaining blood dyscrasias can be grouped for orientation according to the age periods of their most frequent incidence: newborn, infancy and childhood. The diagnostic features of erythroblastosis fetalis and of hemorrhagic disease of the newborn are apparent at birth or shortly thereafter. The anemia of prematurity, iron deficiency anemia and hypoplastic or congenital aregenerative anemia become noticeable during the earlier months of infancy. Megaloblastic or macrocytic anemia of infancy and hemophilia occur either during the first few months of life or in the older infant. The severe forms of hereditary hemolytic anemias, which consist of Mediterranean anemia, congenital hemolytic jaundice and sickle cell anemia, present themselves initially for diagnosis early in infancy, whereas the manifestations of the moderate forms develop more slowly and are noticed in later infancy or early childhood. Aplastic anemia and congestive splenomegaly (Banti's) disease and other disorders associated with splenomegaly and anemia, such as Gaucher's disease and leukemia, are encountered in childhood. It must be emphasized that the onset of the blood disorders first recognized in older infants and children precedes by a variable period the time when the distinguishing features of the condition become unmistakable.

NORMAL RANGE OF HEMATIC VALUES IN INFANCY AND CHILDHOOD

Hemoglobin Content and Red Blood Cells.—A primary consideration in diagnosis of the anemia is the designation of normal hematic values during the period of growth. A knowledge of the values for hemoglobin and red blood cells at birth and in the early newborn period are essential in the diagnosis of erythroblastosis fetalis, because there may be considerable variation in the clinical and hematologic manifestations of this disease. There is evidence, however, that normal values vary greatly in different areas and that these fluctuations depend in large measure on the race, geographic location and to a great extent on the technic of estimation.

In general the average hemoglobin level on the first day of life may be regarded as 20 Gm. per hundred cubic centimeters of blood, with values ranging from 18 to 22 Gm., and the red count as 5,500,000 per cubic millimeter, with a range from 5 to 6 million. During the first 2 years of life the hemoglobin content normally ranges from approximately 10 to 12.5 Gm. per hundred cubic centimeters of blood, with an average value of 11 Gm. Between 3 and 5 years of age it ranges from 12.5 to 13 Gm., and between 5 and 10 years, from 13 to 13.5 Gm.; during puberty it rises gradually to the adult value of 14.5 Gm. per hundred cubic centimeters. A count of 4 million red cells per cubic millimeter of blood may be regarded as the lower limit of normal for the older infant and child. In normal newborn infants the number of nucleated red cells in the first few days of life ranges from 3 to 10 per 100 white blood cells.

Volume of Packed Red Cells.—In all anemias the measurement of the volume of packed red blood cells by the hematocrit constitutes an important and essential guide for diagnosis and therapy. This determination reflects the total mass of cells in a unit volume of blood and has proved of fundamental value in the study of all anemias, in which considerable alterations occur in the size, shape and thickness of the red blood cells. It has the advantage of being reliable and least subject to error in quantitative interpretation. In iron deficiency anemia, for instance, the extremely low hematocrit measurement reflects the state of anemia more accurately than does the more moderate reduction in the number of red blood cells. Also in the asymptomatic person with the trait of Mediterranean anemia the volume of packed red cells frequently remains at the same level in spite of wide fluctuations in the number of red cells.

For measuring the volume of packed red cells with the use of blood from the finger, the method described in previous publications[1] has continued to prove reliable; it is particularly useful in infants and children, in whom repeated venipuncture is undesirable. The values secured with this method coincide with those obtained with venous blood.

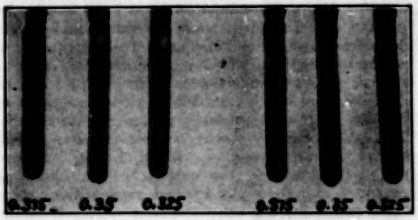
Because of the variations noted in available studies, it is difficult to state the optimum packed cell volume for different age groups. As a working basis, a hematocrit reading of 36 per cent constitutes the lower limit of normal for infants and children and one of 40 per cent, the minimum for older groups.

The Fragility Test.—The resistance of the red corpuscles to varying dilutions of hypotonic solution of sodium chloride constitutes an important laboratory procedure in the diagnosis of the anemias and is especially useful in the differentiation of the hemolytic group. The response of blood cells in the fragility test does not necessarily reflect their reaction within the circulating blood, where conditions of isotonicity prevail. The resistance of the red cells to hemolysis in the

1. (a) Smith, C. H.: A Method for Determining the Sedimentation Rate and Red Cell Volume in Infants and Children with Use of Capillary Blood, Am. J. M. Sc. 192:173 (July) 1936; (b) Sedimentation Rate in Nutritional Anemia of Infants and Children, Am. J. Dis. Child. 56:510 (Sept.) 1938.

fragility test depends undoubtedly on a number of intrinsic factors, which involve the structure and properties of the cell envelope. It constitutes, however, a useful gross index of the relative thickness of the major number of red cells in the sample of blood to be tested. If the red cell envelope is small in relation to its volume, as in the thick red cells or spherocytes of familial hemolytic jaundice, the resistance is decreased. Increased resistance to hemolysis is noted when the bulk of red blood cells possess relatively large surfaces in comparison with their substance, as occurs in the thin red cells of Mediterranean anemia and in iron deficiency anemia. Sickle cells are also more resistant to hypotonic saline solutions than are normal cells.

Increased fragility of the red cells in hypotonic solutions of sodium chloride as compared with the fragility of normal blood occurs in congenital hemolytic jaundice and occasionally in acute hemolytic anemia associated with infection and ingestion of drugs. Decreased fragility with complete hemolysis in solutions below 0.3 per cent sodium chloride characterizes the blood of sickle cell anemia, mild and severe forms of Mediterranean anemia and iron deficiency anemia.



Screening test for erythrocyte fragility employing blood from the finger. The three tubes on the left contain blood from a person with the trait of Mediterranean anemia and show decreased fragility. The corresponding tubes on the right contain blood from a control and show normal hemolysis.

In studying large groups of patients suspected of having one of the forms of Mediterranean anemia several technical difficulties were encountered, which interfered with the frequent performance of fragility tests, especially in several members of a family. The difficulties involved the preparation of a large number of tubes containing serial dilutions of hypotonic solution of sodium chloride, the use of venous blood in small children and the need for a control in each period.

A screening test was therefore devised utilizing blood from the finger and three dilutions of hypotonic solution of sodium chloride, which experience had shown to offer information of a decisive diagnostic character. These were the tubes containing 0.375 per cent, 0.35 per cent and 0.325 per cent of sodium chloride. The method as here outlined is not meant to replace the routine fragility test but was devised solely as a gross method in screening out large numbers of patients suspected of having Mediterranean anemia. With the use of blood from the finger controls are readily available, and in normal persons the degree of hemolysis in the three tubes is as follows: with 0.375 per cent solution of sodium chloride, 3 plus; with 0.35 per cent, 3 or 4 plus, and with 0.325 per cent, 4 plus. Two or three drops of blood from the finger depending on the severity of the anemia, are obtained by deep puncture and added to each of the three tubes, each of which contain 2 cc. of solution of the prescribed concentrations of sodium chloride. After thorough mixing of blood and solution, the tubes are allowed to stand in a refrigerator until sedimentation has occurred. The degree of hemolysis and the residue of unhemolyzed red cells are compared with the same factors in the blood of a normal control treated in the same manner. If any clotting occurs the tube is centrifuged at low speed for a few minutes and the degree of hemolysis in the supernatant fluid is compared with that found in the corresponding tube of the control.

In seventy-five comparative tests with finger and with venous blood the extent of hemolysis in each of the tubes closely approximated that in the corresponding tube. When any discrepancy occurred venous blood was found to be slightly more fragile than finger blood. The usefulness of this procedure has also been demonstrated in a small group of cases which included congenital hemolytic jaundice, sickle cell anemia and iron deficiency anemia. The results with this method will be reported more fully later.

The Reticulocyte Count.—The reticulocyte count reflects the state of activity of the bone marrow; hence this determination provides a useful guide in the diagnosis of both deficiency and hemolytic anemias and in gaging the response to treatment. Normally from 0.5 to 1.5 per cent of the red blood cells are reticulated, and levels below 0.5 per cent represent an inactive bone marrow. A persistent depression in the percentage of the reticulocytes in spite of treatment occurs in aplastic and in hypoplastic anemia. In anemia due to a deficiency a reticulocyte response from previously low levels follows appropriate treatment. In the hemolytic anemias the values for reticulocytes are consistently elevated, and the high levels which are sustained prior to and without treatment represent intensified activity of the bone marrow. A simplified procedure previously described [20] has been employed, which has been adapted from standard methods and requires no preliminary preparation of slides or other devices.

Icterus Index.—Blood destruction may be gaged by the level of the biliary pigments in the plasma and by the quantitative estimation of the urobilin in the stools. Intensity of the pigmentation of serum is readily measured by the icterus index, which usually ranges from 4 to 6. In hemolytic anemias the values range between 15 and 25. A greatly elevated icteric index points to hepatic damage and biliary obstruction rather than to jaundice due to hematic destruction alone.

EXAMINATION OF THE BONE MARROW BY STERNAL PUNCTURE

Investigation of the bone marrow by sternal puncture constitutes an invaluable laboratory aid in association with a careful examination of the peripheral blood. Information as to the normal range for the total nucleated cell count, the differential percentages for each type of cell, the variability in different age periods and the extent of individual fluctuations in bone marrow obtained by sternal aspiration is still limited. Despite these restrictions certain qualitative and gross quantitative alterations can be ascertained and a rough estimate made of hypoplasia or hyperplasia in the bone marrow and of the predominance of one or more types of cells.

Normal Bone Marrow.—The figures in table 2 represent the approximate range and average values of the cellular elements which one may expect to find in samples of the bone marrow obtained from normal infants and children. The higher lymphocytic percentages have been noted in normal infants beyond the neonatal period.

Bone Marrow in the Anemias.—The individual cellular constituents in the bone marrow are in such close proximity to each other that it is difficult to affect one element independently of the other. This total stimulation is best observed in the hemolytic anemias and most regularly in acute hemolytic anemia. In the latter, regeneration of the red blood cells is associated with an increase in the number of granulocytes and platelets. The reverse occurs in aplastic anemia, in which values for the three types of blood cells are depressed simultaneously. However, other factors must operate in addition to anatomic proximity, since involvement of a single type of cell may occur. This is illustrated in hypoplastic anemia, in which the production of red blood cells is inhibited without equal depression of the other cellular elements. Similarly, selected hyperplasia occurs in iron deficiency anemia and in chronic loss of blood, in which the normoblasts and their immediate precursors alone are primarily increased.

In the group of hemolytic anemias, which comprise congenital hemolytic jaundice, acute hemolytic anemia, sickle cell anemia and Mediterranean anemia, the bone marrow is hyperplastic and there is an increased proliferation of normoblasts and to a lesser extent of erythroblasts. Granulopoiesis may be active especially in acute hemolytic anemia. In iron deficiency anemia and in chronic hemorrhagic anemia the bone marrow is similarly hyperplastic; values for normoblasts are greatly elevated, but granulopoiesis is normal. In acute hemorrhage, however, the activity of the myeloid elements is also increased. The increase of the nucleated red cells in these disease processes in excess of 50 per cent of all the nucleated elements in the marrow constitutes an important diagnostic feature.

Aplastic anemia is associated with hematic observation of profound anemia, leukopenia, neutropenia and thrombocytopenia. The bone marrow shows a progressive decrease in cellularity, and there is a sharp reduction in the myeloid elements, megakaryocytes and nucleated red cells with a relative increase in normal lymphocytes. Occasionally acute lymphoblastic leukemia in the leukopenic stage may simulate aplastic anemia, and diagnosis is difficult without histologic examination of the bone marrow. Sternal aspiration in patients with leukemia will reveal a cellular bone marrow in which the normal nucleated elements are replaced by lymphoblasts and lymphocytes. With the progressive reduction in the number of platelets, hemorrhages occur in aplastic anemia which may simulate thrombocytopenic purpura. In the latter disease the bone marrow reveals hyperplasia of the megakaryocytes with values ranging from 200 to 300 per cubic millimeter.

Hypoplastic anemia differs from aplastic anemia in that the formation of red blood cells is depressed without equal involvement of the granulocytes or platelets. Aspiration of the bone marrow reveals pronounced reduction in the numbers of nucleated red cells as well as an increase in the numbers of primitive cells, or hematogones, and of eosinophilic leukocytes. The bone marrow in macrocytic or megaloblastic anemia of infancy [4] reveals a megaloblastic type of erythropoiesis and changes in the granulocytes resembling those observed in pernicious anemia.

THE ROENTGENOGRAM IN DIAGNOSIS OF HEMATIC DYSCRASIAS

The greater value of the roentgenogram in the diagnosis of hematic dyscrasias in earlier periods of life can be related to the developmental features of the bone marrow. Only with the appearance of nonfunctioning yellow marrow in the older child and its extension in the young adult is a potential reservoir created for the formation of blood when the demand for hematic regeneration is increased. In early infancy, however, the need for increased formation of blood arising from anemia due to infection or associated with specific hematic diseases may necessitate the reactivation of extramedullary fetal sites. When there is need beyond this for the formation of blood, the marrow expands by absorption or atrophy of bone trabeculae and of the cortex, and the visualization of these changes in the roentgenogram is utilized in diagnosis.

Leukemia may be difficult to distinguish from other hematic dyscrasias in the stage when anemia is associated with leukopenia and minimal enlargement of the spleen and lymph nodes. The roentgenogram fre-

TABLE 1.—*Significant Normal Values in Diagnosis of Anemias of Infancy and Childhood*

Hemoglobin	1st day	20 Gm. (18 to 22 Gm.)
	2 weeks	17 Gm.
	1st 2 years	11 Gm. (10 to 12.5 Gm.)
	3 to 5 years	12.5 to 13 Gm.
	6 to 10 years	13 to 13.5 Gm.
	10 years to puberty	13.5 to 14.5 Gm.
Red blood cells	1st day	5,500,000 (5 to 6 million)
	3d week	3,500,000
	Older infant and child	4,500,000 per cu. mm. lower limit of normal
Nucleated red cells	Average at birth ranges from 3 to 10 per 100 white cells	
Reticulocytes	0.5 to 1.5%; (below 0.5% in aplastic and hypoplastic anemia; increased in hemolytic anemia; in deficiency anemia rise from low to high levels with treatment)	
Volume of packed red cells	Infants and children	30% is lower limit of normal
	Older age groups	40% minimum
Icterus index	Normal, 4 to 6 units; (hemolytic anemias, 15 to 20%)	
Fragility test	Normal range 0.425 to 0.325% sodium chloride; (increased fragility in congenital hemolytic jaundice and in some cases of acute hemolytic anemia; decreased fragility in sickle cell anemia, Mediterranean anemia and in iron deficiency anemia)	

TABLE 2.—*Relative Number of Nucleated Cells in Normal Bone Marrow (Sternal Aspiration)*

Total nucleated cell count approximately 100,000 to 150,000 per cu. mm.

	Range, %	Average, %
Myeloblasts	1 to 5	2
Myelocytes (including promyelocytes)	10 to 35	20
Nonsegmented polymorphonuclears (including metamyelocytes)	15 to 30	20
Segmented polymorphonuclears	5 to 20	25
Lymphocytes	5 to 25	12
Nucleated red cells (principally normoblasts)	15 to 30	20
Plasma cells	Occasional	
Monocytes	Occasional	
Reticulum cells	Occasional	
Hematogones	Occasional	
Megakaryocytes	10 to 25 per cu. mm.	

4. Zuelzer, W. W., and Ogden, F. N.: Megaloblastic Anemia in Infancy: A Common Syndrome Responding Specifically to Folic Acid Therapy, Am. J. Dis. Child. 71:211 (March) 1946.

quently throws light on the underlying pathological process in leukemia, disclosing generalized or local rarefaction, focal areas of absorption of the bone and of periosteal elevation. The extensive erythrogenesis is seen in Mediterranean anemia, familial hemolytic jaundice and sickle cell anemia. Pronounced skeletal changes appear with greatest regularity in Mediterranean anemia and similar changes but to a lesser extent are observed in the other members of this group. The roentgenogram in Mediterranean anemia reveals the evidence of extreme hyperplasia of the bone marrow by osteoporosis, thinning of the cortex, trabecular atrophy, coarse reticulation with regeneration of new bone, which is a later development in the disease, and thickening of the skull. Lateral views of the skull show an enlarged diploic space which is finely granular or mottled or striated. The vertical striations give the appearance of "hair standing on end," which seems to extend beyond the outer table. The earliest signs are observed in the small bones, particularly in the metacarpals and metatarsals, and reveal osteoporosis and expansion of the medullary cavities, producing a rectangular instead of the normal concave appearance. The inital osteoporotic process which occurs in infancy and early childhood is succeeded by osteosclerosis, in which new bone is formed and is represented in the roentgenogram by trabeculation and coarse reticulation. Osteosclerosis with cortical thickening in the large bones constitutes an outstanding feature of sickle cell anemia in adults, although its evolution from a previous osteoporotic phase has infrequently been noted.

TABLE 3.—*Diagnostic Features of the Bone Marrow (Sternal Puncture) in Anemias of Infancy and Childhood*

Hemolytic group	
Erythroblastosis fetalis Congenital hemolytic jaundice Sickle cell anemia Mediterranean anemia Acute hemolytic anemia	Hyperplastic marrow with increase of nucleated red cells—chiefly normoblasts; granulopoiesis may also be active
Iron deficiency anemia	Hyperplastic marrow with increase in normoblasts; granulopoiesis unchanged
Hemorrhagic anemia	Hyperplastic marrow with increase in nucleated red cells, chiefly normoblasts; granulopoiesis active in acute hemorrhage and unchanged in slow and chronic loss of blood
Megaloblastic anemia of infancy	Pattern similar to pernicious anemia in relapse; megaloblastic type of erythropoiesis and changes in granulocytes resembling pernicious anemia
Aplastic anemia	Usually decreased cellularity to acellular; sharp reduction in myeloid elements, megakaryocytes and normoblasts and increase in lymphocytes
Hypoplastic anemia	Hypoplastic marrow with pronounced depression affecting normoblasts mainly; primitive cells (hemocytogones) and eosinophils increased
Lymphatic leukemia	Replacement of normal nucleated elements by lymphoblasts and lymphocytes
Thrombocytopenic purpura	Moderate hyperplasia of marrow with increase in megakaryocytes

HEREDITARY FACTORS AS AN AID IN DIAGNOSIS

The accurate diagnosis of diseases of the blood in younger subjects frequently requires a consideration of hereditary factors. In certain of the hematic diseases a clue to causation and diagnosis is obtained by a search for similar hematologic abnormalities in the mother, by an investigation of the possible interaction of immunologic factors between mother and fetus which affect hematopoiesis and by a study of the blood of parents and siblings of the affected child for the presence of the trait.

The diagnosis of hypochromic microcytic anemia in an infant between the age of 3 and 6 months on the basis of inadequate storage of iron in fetal life is suggested by a history of iron deficiency in the mother during pregnancy. Congenital thrombocytopenic purpura in infants may be considered when the disease has been present in the mother. Occasionally, thrombocytopenia in the mother has not been associated with serious clinical manifestations and this condition has been discovered while investigating the source of purpura in the infant.

Probably the most important element in the diagnosis of erythroblastosis fetalis depends on a genetic study of the Rh blood factor in the infant and its parents. Typing of the blood for the Rh factor has become an essential diagnostic procedure. In the majority of cases the red cells of the father and of the infant possess the Rh factor and the mother lacks it. In the smaller group of Rh positive mothers, the Hr and the A and B agglutinogens may represent the responsible immunizing agents.

Sickle cell anemia, hemolytic jaundice and Mediterranean anemia are familial diseases in which the hereditary trait may be recognized by appropriate hematologic studies. The constitutional nature of these diseases is reflected in the comparatively high incidence in members of the same family.

The diagnosis of these diseases in a child with an obscure anemia of moderate severity can often be made earlier in its course and useless therapy avoided by the detection of the trait in the parents and siblings. In Mediterranean anemia, for instance, the most important element in the diagnosis of the milder form is the discovery of qualitatively similar alterations in the blood of other members of the same family. These persons are asymptomatic and are either mildly anemic or without anemia. Regardless of the hemoglobin level their blood shows hypochromic macrocytes, stippled erythrocytes, polycythemia, increased resistance of the red cells to hemolysis in hypotonic solutions of sodium chloride and, less frequently, target and oval cells. The presence of basophilic stippling may be so pronounced in the mild form of the disease as to confuse the condition with lead poisoning.[4] On the basis of previous studies [5] and of an investigation now in progress the evidence is conclusive that in every family with a child severely affected with Mediterranean anemia and requiring periodic transfusions of blood both parents revealed evidence of the disease. As a corollary the important principle may be affirmed that the designation of a hematic dyscrasia as a moderate or severe form of Mediterranean anemia should not be made unless at least one of the parents shows the trait of the disease.

5. Dameshek, W.: Familial Mediterranean Target-Oval Cell Syndromes, Am. J. M. Sc. 208:643 (May) 1943. Smith, C. H.: Familial Blood Studies in Cases of Mediterranean (Cooley's) Anemia, Am. J. Dis. Child. 65:681 (May) 1943. Valentine, W. N., and Neel, J. V.: Hematologic and Genetic Study of the Transmission of Thalassemia, Arch. Int. Med. 74:185 (Sept.) 1944.

Rundles and Falls[6] recently described an anemia affecting the male members of two families of non-Mediterranean origin which was transmitted by females without anemia. Many of the latter had large spleens, and examination of their blood revealed minor abnormalities of the red cells.

DIAGNOSTIC CHARACTERISTICS OF THE BLOOD SMEAR

The examination of the blood smear represents the most direct means for observing the effect on morphology of the factors involved in the pathogenesis of a particular form of anemia. In enumerating the changes in the blood cells it should again be emphasized that except for sickle cells and spherocytes there are no specific cells which may be considered pathognomonic of a particular disease. Target cells, oval cells, hypochromic macrocytes and basophilic stippling appear in certain stages of many anemias and therefore cannot be regarded as a specific hematologic feature of a single disease. They are of diagnostic value only when they are considered in conjunction with pertinent information obtained from other sources. When anemia results from direct bone marrow depression, such as occurs in aplastic and hypoplastic anemia or the marrow cell displacement of leukemia, the red cells are both normochromic and normocytic, and anisocytosis, poikilocytosis and achromia are minimal.

In erythroblastosis fetalis, the acute phases of congenital hemolytic anemia, sickle cell anemia, Mediterranean anemia, acute hemolytic anemia and acute posthemorrhagic anemia, the blood film reveals certain common features. These reflect increased activity of the bone marrow and include reticulocytosis, nucleated red blood cells, leukocytosis, increased granulocytes, immature myeloid cells and in certain instances (acute loss of blood and acute hemolytic anemia) an elevation in the number of platelets.

The hematic observations that characterize each form of anemia are summarized in table 4. Occasionally the blood films in well defined conditions resemble each other so closely that corroborative evidence from auxiliary sources is required to establish a diagnosis. This overlapping is exemplified in certain children with sickle cell anemia in whom the typical cells are demonstrated with difficulty in the fixed smear or with sealed preparations of fresh blood. In the anemic patient with this disease the smear reveals target and oval cells, numerous hypochromic macrocytes and occasional stippled cells. When sickle cells are absent, differentiation of this disease from Mediterranean anemia at a comparable stage is difficult. Reexamination with various technics to demonstrate sickling and study of the blood of other members of the family for the distinguishing features of either disease may be necessary to separately classify the two conditions.

THERAPEUTIC RESPONSE AS AN AID IN DIAGNOSIS

The insidious onset of many of the anemias of early life renders their diagnosis difficult before specific criteria are established. Until the important features have developed, the response to a therapeutic agent often serves to eliminate certain conditions and focus attention on others. Since the low hemoglobin value is the outstanding feature of the anemias in early life, the observed response to a therapeutic trial with an iron salt constitutes an ideal preliminary procedure for purposes of differential diagnosis. For example, when iron in sufficient dosage is administered to an infant or young child with anemia of moderate severity, the absence of a reticulocyte response and a failure of the hemoglobin to return to normal values within three to four weeks suggest continued activity of an acute or chronic infection or of some other exogenous factor or that the diagnosis of anemia on a deficiency of this mineral alone is to be questioned. By the employment of this principle, cases of Mediterranean anemia have been uncovered in early infancy when the clinical, roentgenographic and hematologic features were still equivocal. Similarly, anemic syndromes resistant to therapy with liver and iron suggest the possibilities of aplastic or of hypoplastic anemia. On the other hand a satisfactory response to folic acid or to liver extract in an infant with a macrocytic anemia contributes important confirmatory evidence for the diagnosis of megaloblastic anemia.[4]

TABLE 4.—*Diagnostic Features of the Blood Smear in Anemias of Infancy and Childhood*

Erythroblastosis fetalis	Hyperchromic macrocytes, nucleated red blood cells
Hemorrhagic anemia *	Acute blood loss; normochromic and normocytic red blood cells; chronic blood loss; hypochromic microcytes
Iron deficiency anemia	Hypochromic microcytes, pronounced central pallor of red blood cells, poikilocytes
Anemia of prematurity	Early normocytic and normochromic red blood cells; later hypochromic microcytes
Megaloblastic anemia of infancy	Extremely large macrocytes, microcytes, occasional nucleated red blood cells, abnormal neutrophils
Aplastic and hypoplastic anemia	Normochromic and normocytic red blood cells
Congenital hemolytic anemia	Spherocytes and large number of reticulocytes
Sickle cell anemia	Sickle cells, target and oval cells, hypochromic macrocytes
Mediterranean anemia †	
Severe type	Extremely large, thin hypochromic macrocytes; nucleated red blood cells; pronounced poikilocytosis and anisocytosis
Mild type or trait	Hypochromic macrocytes, basophilic stippling, polycythemia, target and oval cells

* This applies to phases of hemorrhagic disease of the newborn, hemophilia, thrombocytopenic purpura, to less common hemorrhagic disorders and to nonspecific conditions associated with loss of blood.

† In both types the red blood cells show increased resistance to hemolysis in hypotonic solutions of sodium chloride.

SUMMARY

While many of the anemias of infancy and childhood do not differ greatly from those of the adult, their diagnosis may be attended with difficulty because of peculiarities in this age period. The anemias in early life develop insidiously, and diagnosis may be uncertain before specific criteria are established. Alterations in the blood need to be appraised in the light of the residual effects of fetal and maternal influences on hematopoiesis and of normal changes incident to growth and development. Many of these complexities may be resolved and diagnosis facilitated by coordinating the information obtained from the sources which were described in this paper. The detection of hematic disturbances requires a careful history and the use of simple instruments and technics; and the collection of data and their interpretation lie within the province of every medical practitioner.

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6. Rundles, R. W., and Falls, H. F.: Hereditary (? Sex-Linked) Anemia, Am. J. M. Sc. 211:641 (June) 1946.

PATHOGENESIS OF ANEMIA IN INFANCY AND CHILDHOOD

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Anemia is a pathologic state characterized by a decrease in the amount of hemoglobin per unit volume of circulating blood and resulting in a reduction of the oxygen-carrying power of the blood. Many details regarding the genesis of anemia remain to be settled, but it is clear that the various causative factors capable of producing the anemic state must operate through a few basic mechanisms. An understanding of these mechanisms is essential for the interpretation of blood pictures and for the rational treatment of the anemias of all age groups. The peculiarities of the anemias of infancy and childhood are due not to fundamental differences in the pathogenic mechanisms but to the peculiarities of the infantile organism itself, especially growth and metabolism, nutrition and susceptibility to infection, which modify and favor the development of anemia. While stressing the significance of these special features, a discussion of the pathogenesis of the anemias of infancy must be based on principles applicable to anemia in general.

The blood, more specifically the circulating hemoglobin, may be compared to a reservoir in which a constant level is maintained by regulatory mechanisms which govern the intake and outflow. The intake is determined by the production and release of hemoglobin-containing cells by the marrow organ, which is the only normal source of supply in extrauterine life. The outflow represents destruction and removal of erythrocytes from the circulation with subsequent breakdown of hemoglobin in the reticuloendothelial system, especially the spleen. Under physiologic conditions the production and destruction of hemoglobin are balanced, and in adult life both the size and the level of the reservoir remain constant. In childhood, especially in infancy, however, the production of hemoglobin must not only replace physiologic losses but also furnish new material as the total blood volume increases with the rapid growth of the body, so that the absolute size of the reservoir is greatly expanded while its level remains nearly constant. In the anemic state the level falls because the regulatory mechanisms fail. In the last analysis anemia is always the result of either diminished production of hemoglobin by the marrow or excessive loss of hemoglobin from the circulation or a combination of both. For the purposes of this discussion the two fundamental mechanisms will be considered separately.

DIMINISHED PRODUCTION OF HEMOGLOBIN BY THE MARROW

The role of the marrow in the production of hemoglobin may be viewed under the aspects of cellular regeneration and the synthesis of hemoglobin. Erythrocytes are formed by mitotic division of nucleated precursor cells—erythroblasts—at different levels of cellular development. In the process of maturation the erythroblasts synthesize hemoglobin and cease mitotic activity. The majority of these elements lose their nuclei, pass into the reticulocyte stage and are then ready for delivery into the circulation. The regeneration of erythrocytes is a delicately integrated process, which normally operates far below the maximum capacity of the system. The known facts support the view that this process is regulated within certain limits by the supply of oxygen and that relative anoxia stimulates mitotic division of erythroblasts, while an abundant oxygen supply seems to have the opposite effect.

In fetal life oxygen tension is low and erythropoiesis is highly active. In early infancy a quantitative reduction in erythroblastic regeneration takes place, apparently in response to the improved oxygenation following the change from placental to pulmonary ventilation. This adjustment falls into a period of rapid growth with expansion of the blood volume, which tends to dilute the circulating hemoglobin. The combination of these two factors, decrease in the rate of erythropoiesis and increase in the volume of blood accounts for the relatively low hemoglobin level of the normal infant which is spoken of as the physiologic anemia of infancy. The more pronounced anemia of prematurity is due to an accentuation of these same factors. The growth rate and expansion of blood volume is relatively greater than in the full term infant. The oxygen supply to the tissues of the premature infant may be assumed to be greater than that available to a fetus of comparable conception age. Moreover, the hypothermia and inactivity of such infants suggest a low rate of consumption of oxygen. One would therefore expect an inactive erythropoiesis, and this is borne out by actual studies of the marrow.[1] Blood formation in the premature infant is even less active than that in the full term infant. The anemia of prematurity, like the physiologic anemia of early infancy, is not due to some deficiency but may be considered as the result of these adjustments which are physiologic for the premature infant, as far as anything can be called physiologic in these patients. This view is supported by the observation made repeatedly in the laboratory of the Children's Hospital of Michigan that hemolytic or hemorrhagic episodes which produce a definite demand on the marrow are followed by hyperplasia of the marrow and reticulocytosis of the peripheral blood even in premature infants. This observation indicates that the marrow can respond if the proper stimulus is provided. It should be clear that the administration of iron cannot influence the early phases of the anemia of prematurity although it later can prevent the iron deficiency anemia to which the premature infant is subject after the third month.

The view that the rate of regeneration of the red blood cells is related to the available supply of oxygen is supported by the observations in hypothyroidism, in which the consumption of oxygen in the tissues is abnormally low. The anemia of myxedema is associated with hypoplasia of the bone marrow (a reduction in the number of cell divisions), which has been interpreted as an adjustment to the low oxygen consumption of the hypothyroid state.[2] It is possible that the anemia often seen in scurvy is likewise related to decreased consumption of oxygen, because lack of ascorbic acid interferes with the oxidative process in the body and because hypoplasia of the marrow has been noted in scurvy.[3] However, loss of blood and iron deficiency

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usually complicate infantile scurvy, and the evidence in regard to the anemia of scurvy is as yet conflicting.[4]

Reduction in the supply of oxygen to the marrow is followed by an increase in the rate of regeneration of the red blood cells. It is immaterial whether the anoxia is brought about by decreased atmospheric oxygen pressure, by increased consumption of oxygen in the rest of the body, by circulatory conditions, by impairment of pulmonary ventilation or by anemia. Anoxia is the common denominator of these states and may be considered as the physiologic stimulus for regeneration of the red blood cells. It is doubtful whether erythropoiesis can be stimulated in any other way except through the mechanism of marrow anoxia. At least it has not been shown that normal marrow under normal oxygen tension can be stimulated to increase the production of red blood cells.

Anemia, then, is in itself a stimulus for the marrow. This is illustrated by the changes which follow acute loss of blood. The anemia causes a decided increase in the number of cell divisions among the erythroblasts, i. e., the marrow becomes hyperplastic. As newly formed cells mature and reach the reticulocytic stage they enter the blood, the anemia is alleviated, the oxygenation of the tissues improves and the marrow response subsides. In the previously normal person this sequence of events occurs without any form of therapy. If anoxia of the marrow is prevented or relieved by blood transfusion the response is abolished or proportionately diminished.

The effect of excessive destruction of the blood on the activity of the marrow is the same as that of sudden loss of blood. However, if blood destruction is continuous and severe, as in chronic hemolytic anemias, even maximal activity of the marrow cells may not fully compensate for the loss of hemoglobin and the anemia may persist. If the degree of hematic destruction can be reduced, as may be the case after a splenectomy has been performed, the activity of the marrow decreases as the hemoglobin approaches normal levels.

Such compensatory adjustments require a normally functioning marrow organ. Often, however, impairment of erythropoiesis itself is the primary factor in the development of anemia, and in that case the anoxic stimulus cannot be effective until conditions necessary for normal functioning of the marrow are restored.

This is illustrated by the true marrow deficiency states, in which factors essential for the normal functioning of erythroid cells are lacking. Experimentally a number of such factors have been demonstrated, but thus far only two have proved of practical clinical significance. One is an antianemic principle often referred to as erythrocyte maturation factor, contained in liver and according to recent studies also in folic acid [5] and perhaps identical with the latter. If this factor is not available to the marrow the erythroblasts become abnormal in structure and function. In these pathologic cells, which are generally called megaloblasts, the delicate mechanism of mitotic division is affected.[6] Multiplication is restricted mainly to the most primitive precursor cells. This derangement in the regulation of mitotic activity leads to the apparent paradox of marrow hyperplasia with hypoplasia of the blood, or anemia; few of these primitive megaloblasts mature, and their long maturation period means delay in their delivery to the blood. Such cells as enter the circulation are large because they represent end stages in the development of large primitive cells; hence, anemias of this type are usually macrocytic. Pernicious anemia, the classic example of a deficiency in antianemic principle, seldom occurs in infants [7] and is extremely rare in children. Recent studies of marrow patterns, however, have shown that a temporary deficiency of the antianemic principle is fairly common in infancy. The term megaloblastic anemia has been proposed for this condition.[8] It can arise as the result of dietary deficiency as in so-called goat's milk anemia and also apparently through interference with absorption or utilization of antianemic principle on the basis of infection. Megaloblastic anemia is occasionally seen in children with celiac disease as one of the secondary deficiency states associated with faulty absorption by the gastrointestinal tract. If the missing antianemic factor, whether it be liver principle or folic acid, is supplied, cellular regeneration quickly returns into normal channels, the stimulus of the anemia can lead to an effective response by the marrow and mature cells are again produced in adequate numbers.

Iron deficiency states have a somewhat different effect on the marrow. Iron is an actual building stone of the hemoglobin molecule. The erythrocytes which are produced when adequate amounts of iron are not available to the marrow cells are small and hypochromic, because they contain less than their normal complement of hemoglobin.[9] The erythroid marrow may respond to the anemia and become hyperplastic, but the hemoglobin content of the cells and the hemoglobin level of the blood continues to fall. Soon the red blood cell count also falls, because the hemoglobin-deficient erythroblasts do not mature properly and as a result fewer and fewer cells reach the circulation. When iron is made available, the synthesis of hemoglobin can proceed and the cells again mature in normal fashion.

Obvjously iron can be effective only where an iron deficiency of the marrow exists. This occurs principally after exhaustion of the storage iron in the tissues. The preponderance of iron deficiency anemia in infancy is related to the state of this reserve. The storage iron is scarcely affected by the loss of iron through excretion, which is negligible. The iron liberated in the breakdown of hemoglobin can be used over and over for the formation of blood. In the adult the blood volume and total hemoglobin mass is constant and the iron reserves of the tissues are seldom drawn on except after an actual loss of iron from the body, as in hemorrhage. In the infant the rapid growth of the blood volume requires a considerable increase in total hemoglobin if adequate levels are to be maintained. It has been aptly said that the infant bleeds into its own increasing blood volume.[10] Since the milk diet of early infancy is poor in iron it follows

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that the infant must draw on storage iron for blood formation and live, as it were, on its capital reserve of iron. The smaller the initial deposit and the greater the rate of withdrawal, i. e., the growth rate, the more likely it is that anemia will develop. The premature infant who fails to receive the deposits of iron normally transferred during the latter part of gestation and whose rate of growth is high must soon exhaust the initial reserve of iron. At that time the already existing physiologic anemia of prematurity proper is immediately followed by the hypochromic anemia of iron deficiency. The full term infant whose mother suffered from iron deficiency during pregnancy has a normal hemoglobin level at birth but inadequate stores of iron and is prone to the development of an iron deficiency anemia which is preventable.[11]

The size of the reserve of iron may be materially reduced if early ligation of the cord deprives the newborn of the iron contained in the placental blood and normally converted to storage iron.[12] Such infants are more prone to the development of anemia than if this blood had been allowed to return to the circulation. Depletion of storage iron through chronic loss of blood is an infrequent occurrence in infancy but must be considered in regions where hookworm infection is prevalent. Because of the normal drain on the reserves of iron in infants, even acute loss of blood may be followed by a lasting anemia.

In the full term infant the iron stores available after birth are ordinarily sufficient to allow for the growth of the total hemoglobin mass until they can be replenished by iron from the diet. If food rich in iron is not then made available, anemia will develop on a nutritional basis alone. However, a deficiency anemia due to lack of iron is not necessarily the result of inadequate dietary intake; in fact, purely nutritional anemia is relatively infrequent even in infancy. In most instances infection is a precipitating factor.[13] It may interfere with ingestion or absorption of food iron by producing anorexia, vomiting or diarrhea, but its effect on the utilization of iron is far more direct and profound. Available evidence indicates[14] that in the presence of infection, iron is diverted from the marrow and immobilized in the tissues; hence it is not available for the synthesis of hemoglobin. This is true even for iron administered therapeutically. The infant is dependent on storage iron to a far greater extent than is the adult and thus is more liable to anemia when the marrow is cut off from its supply of iron. It is likely, however, that some infections at least have a still more immediate effect on erythropoiesis and can depress cellular regeneration directly.

Iron therapy is usually ineffective in the presence of continued infection but will nearly always produce remission once the infection is overcome. Whether a deficiency of copper is of clinical significance in human anemias is a question of little importance, because traces of copper are present in ordinary commercial iron preparations.

In Mediterranean anemia the red cells are deficient in hemoglobin; yet this hypochromic anemia is permanently resistant to iron therapy, apparently because iron cannot be utilized. The nature of this disease is not yet fully understood, but the known facts support the theory that the marrow cells are in some way unable to synthesize hemoglobin properly or at least in adequate amounts. The disease is hereditary and at present can best be explained as an inborn error of metabolism which affects the marrow cells.

In contrast to the megaloblastic and the hypochromic anemias, in which qualitative as well as quantitative changes in marrow function are evident, certain anemias are characterized by a simple quantitative reduction in the regeneration of erythroid cells which persists in spite of the increased demand caused by the anemia. These conditions may be designated as hypoplastic and aplastic states. The failure to make new erythrocytes produces a proportionate fall in hemoglobin and in the red blood cell count, and reticulocytosis and other signs of hematic regeneration are lacking. Similar blood pictures, however, are observed in the presence of actual hyperplasia of marrow with the arrest of maturation, when primitive cells are formed but are not released into the circulation.[15] The so-called hypoplastic and aplastic blood pictures can therefore reflect diametrically opposite conditions of the marrow and can be interpreted properly only through a study of the marrow. Therefore the concept of hypoplastic-aplastic states must be based on the process in the marrow rather than on observations in the blood.

Hypoplasia of the bone marrow may involve erythroid elements selectively or may affect all marrow cells. Erythroid cellular hypoplasia is found in anemias associated with a variety of conditions, such as infection, chronic renal disease and malignancy, and will persist until the underlying disease is eradicated.[16] Selective hypoplasia of erythroid marrow cells of completely obscure cause is seen in a rare chronic anemia of children, which appears to be congenital and which bears the name chronic hypoplastic anemia.[17] The production of leukocytes and platelets remains adequate, and the patients can live comfortably as long as transfusions at appropriate intervals provide the necessary red blood cells.

Occupation of the marrow space by such processes as fibrosis, sclerosis, osteopetrosis, metastases and infiltration with Gaucher's cells leads to a different picture. Such marrow as remains is highly active; the blood contains immature cells probably derived from extramedullary sites of blood formation, and the observations in this so-called myelophthisic anemia may simulate those of leukemia. Perhaps the anemia of leukemia is itself such a myelophthisic process;[16] in any event the leukemic cells proliferate at the expense of erythroid elements, and erythropoiesis is often reduced to the vanishing point.

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The term aplastic anemia is customarily reserved for states in which general depression of marrow activity causes leukopenia and thrombopenia as well as anemia. Such cases are extremely infrequent in childhood, and most of the anemias so classified eventually turn out to be leukemias of the so-called aleukemic type.

EXCESSIVE LOSS OF HEMOGLOBIN FROM THE CIRCULATION

In regard to the mechanisms of blood destruction, both physiologic and pathologic, many details remain to be clarified. The anemias characterized chiefly by increased destruction of blood are referred to by the generic term hemolytic anemias. Actually hemolysis in the sense of lysis of the erythrocytic membrane is only one of several mechanisms that may cause destruction of erythrocytes.[19] In the physiologic turnover hemolysis seems to play no part. The consensus is that during their stay in the circulation the erythrocytes are gradually fragmented by the constant if slight mechanical trauma to which they are exposed.[18] The minute remnants are eventually removed by phagocytosis in the reticuloendothelial system, mainly in the spleen. Phagocytosis of whole cells also occurs but is of minor importance, at least under normal conditions.[19]

The rate of destruction of the red blood cells in the absence of disease seems rather constant. I know of no compensatory mechanism whereby it could be decreased. An increase which might be called physiologic occurs in the first few days of life and accounts at least in part for the rapid reduction of the high hemoglobin levels of the newborn.[20] The details of this destructive process remain obscure.

The breakdown of hemoglobin results in the formation of bilirubin and its oxidation product, urobilinogen. With increased blood destruction the plasma bilirubin level tends to rise; but unless the hemolytic process is severe or hepatic function is impaired, excretion of the pigment by the liver prevents the rise to icteric levels, and clinical icterus is thus only a crude measure. Under certain assumptions the total excretion of urobilinogen in stools and urine is a much more delicate measure of the rate of destruction of blood than is the plasma bilirubin level. The total urobilinogen value depends, of course, on the total hemoglobin mass as well as on the turnover and is therefore much smaller in infants than in adults.

Free hemoglobin appears in plasma and urine only if there is hemolysis in the strict sense of the word and then only in the most fulminating conditions. This suggests that in most states associated with increased hematic destruction cellular mechanisms are involved.

Theoretically increased destruction of blood may be due to: (1) increased fragmentation of cells in the circulation; (2) structural anomalies of the red cells, which make them subject to destruction by the reticuloendothelial system; (3) sensitization of red cells, which makes them susceptible to phagocytosis while they are still intact; (4) increased activity of the reticuloendothelial system, causing its cells to engulf normal erythrocytes; (5) direct lysis in the circulation by hemolysins, bacterial toxins and poisons, and (6) parasitic invasion of red corpuscles, as in malaria.

It is uncertain whether all these mechanisms occur and to what extent the various factors may combine in a given type of hemolytic anemia. In most hemolytic states the reticuloendothelial system, and particularly the spleen, seems to be concerned in one way or another, whether as a passive acceptor of already doomed erythrocytes or as the initiator of the destructive process.

Mere evidence of increased blood destruction does not necessarily indicate an essentially hemolytic anemia but may reflect formation of abnormally vulnerable erythrocytes by a poorly functioning marrow. Signs of increased destruction of blood are evident in pernicious anemia, yet this disease is no longer considered as a hemolytic anemia but as a marrow deficiency state. Fragmentation of abnormal red corpuscles in the circulation is thought to account for the increased blood destruction in Mediterranean anemia,[21] and this disease is usually classified with the hemolytic anemias. But there is reason to consider a metabolic disturbance in marrow function as its essential feature and the fragmentation of the erythrocytes as incidental.

Exaggerated blood destruction is undoubtedly the significant mechanism in congenital hemolytic icterus and sickle cell anemia. The two diseases have many features in common. Both are constitutional anomalies characterized by hereditary transmission, exaggerated destruction of blood in the reticuloendothelial system and an anomalous structure of the mature erythrocytes. In congenital hemolytic icterus the erythrocytes are round instead of biconcave and in some way more susceptible to destruction by the reticuloendothelial system, notably the spleen. This abnormality is congenital and hardly due to substances elaborated within the spleen, since it persists after splenectomy. The fault lies with the cells themselves rather than with an abnormally active organ of destruction, as shown by the observations that cells from normal donors transfused to patients with congenital hemolytic icterus survive whereas the patient's cells disappear rapidly from the circulation of healthy persons.[22] However, since the abnormal cells are destroyed mainly by the spleen, removal of the spleen greatly decreases the rate of blood destruction. In sickle cell anemia the property of the red blood cells to sickle does not in itself account for the destruction of blood, because persons without anemia may have the sickle cell trait. It is uncertain whether the difference is due to a more pronounced abnormality in erythrocytic structure, as suggested by the more decided and more rapid sickling tendency of the cells in the anemic patients, or to greater activity of the destructive mechanisms. Because of the equivocal results of splenectomy in sickle cell anemia such mechanisms are thought to be widely distributed in the body. It has been observed, however, that immediate if only temporary cessation of all evidence of hemolysis occurs after splenectomy in sickle cell anemia quite comparable to the effect of this operation in congenital hemolytic icterus.[23]

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The so-called acquired hemolytic anemias, acute and chronic, are still obscure in their genesis. Hemolysins have been demonstrated in some cases [24] but not in others. Sensitization of the red corpuscles may play a part, as in cases in which the hemolytic anemia follows infection after a latent interval. Certain chemical agents may also produce hemolysis in this manner. The sulfonamide compounds, for example, have no hemolytic effect in the test tube in concentrations comparable to those attained in the blood by therapeutic doses and do not cause hemolysis in normal persons. The infrequent instances of hemolytic anemia after sulfonamide therapy may therefore be related to sensitization of the erythrocytes or of the reticuloendothelial system or of both. In the acquired hemolytic anemias the spleen may not be primarily overactive but may act merely as an acceptor of altered erythrocytes, which might otherwise survive. Reduction of the destructive potential of the reticuloendothelial system by splenectomy may therefore be beneficial and at times lifesaving, but its effects are less predictable in acquired than in congenital hemolytic anemia.

Isoimmune bodies affecting the erythrocytes in the circulation are responsible for the acute hemolysis which follows the transfusion of mismatched blood. The A or B agglutinins are usually the effective agents, but antibodies of the Rh type may cause similar reactions.[25] The role of maternal anti-Rh substances in producing the hemolytic anemia of erythroblastosis in the infant is now firmly established,[26] whereas proof that anti-A or anti-B agglutinins of the mother can produce anemia in the offspring is less convincing.

It is not generally appreciated that there is a fundamental difference in the mechanisms of transfusion reactions and erythroblastosis. In transfusion reaction the donor cells are affected by the recipient's antibodies, while in erythroblastosis the patient's own cells are exposed to the effects of immune bodies. It is likely that the effect of the anti-Rh substances is not limited to the red corpuscles but affects other tissues as well and that this accounts for many of the manifestations of erythroblastosis which cannot be explained by hemolysis alone.

Bacterial toxins, apart from a possible effect on the bone marrow, may have a hemolytic action in the test tube and apparently also in the body. This is especially true for infections due to hemolytic streptococcus and Clostridium welchii. Recent studies seem to indicate, however, that in most of the anemias associated with infections the role of hemolysis is negligible compared to the effect on the production of red blood cells.[14a] The anemia which follows extensive burns is apt to be hemolytic in character and is thought to be due to endogenous poisons, perhaps protein cleavage products which in some way sensitize or destroy red blood cells.

This discussion is not intended to present a complete review of the pathogenesis of all types of anemia. The purpose of this presentation was to furnish basic concepts on which the practical management of anemia can be oriented.

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CLASSIFICATION OF ANEMIA IN INFANTS AND CHILDREN

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A complete classification of anemia as it is encountered in all age groups must include morphologic, etiologic and clinical considerations. For the purposes of a symposium such as is being conducted today it seems important to simplify the subject as far as possible so that the discussion may be of value to the practicing physician. For this reason a classification is presented in which the causes of anemia are arranged in the order of their occurrence in a group of hospital patients. This grouping is slightly different from the order in which Dr. Zuelzer has discussed the "Pathogenesis of Anemia." Although it is incomplete, almost all cases of anemia may be placed in one of its categories.

Analysis of 1,500 consecutive admissions to the Boston Floating Hospital was made to determine the incidence of anemia in hospital practice. It was found that 514 patients, or 34 per cent, showed a definite anemia with an erythrocyte count of less than 4,000,000 per cubic millimeter or a hemoglobin percentage below 70. It should be pointed out that the Boston Floating Hospital is largely charitable and that most of the patients are unable to pay the costs of medical care. The hygienic and dietary background of such a group of children is not comparable to that of patients under the care of private physicians. Furthermore, only those patients with severe anemia and those with unusual conditions received the careful consideration of the hematologist.

TABLE 1.—*Incidence of Anemia in 1,500 Patients Admitted to Boston Floating Hospital*

Age, Years	Number of Patients	Per Cent Anemic
0 to ½	227	28
½ to 1	178	47
1 to 2	240	51
2 to 5	285	34
5 to 12	560	22
Total	1,500	34

The incidence of anemia in these 1,500 patients is shown in table 1. The second year of life is the period in which there is the greatest incidence of anemia, about 51 per cent. Approximately 45 per cent of the children under 2 years of age and 25 per cent of those between ages 2 and 12 were anemic. The etiologic factors responsible for the anemia in the 514 patients were determined as far as possible. The anemia was secondary to infection in about half of the cases (table 2). I am unable to present figures showing the bacterial agents or the locus of the infections involved in these cases. Other factors which have been discussed by Dr. Zuelzer seemed to be of greater importance in the occurrence and the severity of the anemia in the individual instances.

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In 92 per cent of the 514 patients with anemia the diminution in the hemoglobin and erythrocyte values were the result of infection, dietary deficiency, prematurity or some combination of these three factors. In the remaining 8 per cent the anemia was associated with congenital and familial conditions, acquired hemolytic states, primary hematic diseases and the other less common causes of anemia.

TABLE 2.—*Etiologic Factors in 514 Cases of Anemia*

	Number of Cases	Per Cent
Infection	232	49
Deficient diet	69	13
Prematurity	11	2
Combinations of foregoing	139	29
Miscellaneous	43	8

The classification in table 3 is arranged on an etiologic basis, more or less in the order of frequency of the etiologic factors. This is not offered as an inelastic classification but as a practical working basis for use in diagnosis and treatment.

The anemia associated with infection may be of three general types dependent on the mechanisms concerned in its production: (1) hypoplastic or aplastic anemia (diminished production of erythrocytes, the so-called toxic suppression of the bone marrow); (2) hemolytic anemia (increased destruction of circulating erythrocytes), and (3) secondary thrombopenic purpura (diminished production or increased destruction of blood platelets). In individual instances there may be all combinations of these mechanisms with resulting differences in the clinical manifestations.

Dietary anemia is most commonly the result of iron deficiency during either the prenatal or postnatal period due to an inadequate supply of iron-containing foods in the diet or a failure in absorption or utilization of iron.

TABLE 3.—*Anemia in Infants and Children*

1. Anemia secondary to infection
2. Dietary anemia (nutritional or alimentary anemia)
   Iron deficiency during:
   (a) Prenatal period
   (b) Postnatal period
3. Physiologic anemia of prematurity
4. Congenital and familial anemias:
   (a) Congenital hemolytic jaundice
   (b) Sickle cell anemia
   (c) Mediterranean anemia
5. Erythroblastosis (acquired hemolytic states)
6. Primary diseases of the blood:
   (a) Aplastic anemia
   (b) Purpura
   (c) Hemophilia
   (d) Leukemia
   (e) Lymphoblastoma (Hodgkins disease, lymphoma, etc.)
7. Anemia secondary to hemorrhage
8. A. Anemia associated with chemical poisons, such as benzene, lead, acetanilid and sulfonamide compounds
   B. Anemia associated with parasitic infection
   C. Anemia associated with neoplasms

In most instances there is hypochromia and microcytosis, and this type of anemia is frequently classified as hypochromic microcytic anemia. However, there may be a deficiency of the erythrocyte-maturing factor found in the liver, resulting in a macrocytic type of anemia which resembles pernicious anemia in many respects and which responds to folic acid.

The anemia of prematurity is physiologic in nature and is simply in a more pronounced degree the anemia which occurs in all infants during the neonatal period. The anemia is in proportion to the degree of prematurity, is severest at the third month of life and tends to disappear by the seventh month. The most important implication of this condition is that it sets the stage for the development of a more serious type of anemia if the infant suffers infection or dietary deficiency.

The congenital anemias include those conditions in which there is a congenital anomaly of the blood-forming organs which results in the production of abnormal erythrocytes. Although there is evidence of increased hemolysis in most instances, the fundamental disorder is the faulty formation of cells. These diseases may be racial and familial as well as congenital.

The fifth division of this classification, erythroblastosis, could properly be labeled acquired hemolytic states. In this case it would include other rarer conditions in addition to the hemolytic anemia of the neonatal period, which is on the basis of incompatibility of the blood groups of the mother and the infant.

The primary hematic diseases, hemorrhage and other miscellaneous causes of anemia are rare in infancy and early childhood but must be considered as possible etiologic factors in cases of obscure origin.

TREATMENT OF ANEMIAS IN INFANCY AND CHILDHOOD

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The treatment of anemia at any age period must inevitably be concerned with etiologic and pathogenetic factors. Rational therapy is possible only when such factors are properly evaluated. Dr. Zuelzer has discussed the basic mechanisms by which anemia is produced in infants and children. Dr. Smith has indicated methods by which these can be detected, and Dr. Baty has grouped the anemias according to their combined pathogenetic, etiologic and clinical characteristics.

The significant point established in the discussion is that the peculiarities of the anemias of infancy and childhood are not due to a fundamental difference in the pathogenic mechanisms but to anatomic, physiologic and clinical features of the infantile organism which condition the response to the various etiologic factors. Some of these features are more important at one age period than at another. Because of this fact therapeutic principles applicable to anemia in general must be related to the modifying influences of the age period and the periods of life in which they occur.

ANEMIA IN THE NEWBORN (BIRTH TO ONE MONTH OF AGE)

Anemia occurring in the neonatal period (birth to 1 month of age) may be due to several factors but is usually on the basis of loss of blood or increased hematic destruction. The symptom complex known as hemolytic anemia of the newborn, or erythroblastosis fetalis, is the most prevalent and is most effectively treated with Rh-negative blood, especially during the first two weeks of life. The amount and frequency of the transfusions should be determined by the patient's general condition and the degree of anemia.

Read in a symposium on "Anemia in Infancy and Childhood" before the Section on Pediatrics at the Ninety-Fifth Annual Session of the American Medical Association, San Francisco, July 3, 1946.

Generally, a level of 3 million red blood cells and a hemoglobin of 8 Gm. are the minimum values to be achieved, and 10 cc. of blood per pound of body weight is the usual amount given at one time. In cases in which Rh-negative donors are not available blood from Rh-positive donors may be used if the plasma is separated and the red cells are washed and resuspended in isotonic solution of sodium chloride. The transfusion of Rh-positive blood without this preparation has been advised by some, but jaundice is often intensified and recovery is slower than with Rh-negative blood. Diamond has shown that many of the baby's red blood cells are bound to the so-called blocking antibody and that these are capable of agglutinating two or three times as much additional Rh-positive blood. This phenomenon may be demonstrated by a slide test devised by Diamond.

In all patients with severe anemia at any age period requiring frequent transfusions of blood Rh typing should be done, because an Rh-negative recipient may develop a sufficient anti-Rh agglutinin titer to cause a hemolytic reaction when Rh-positive blood is frequently administered. While anti-Rh agglutinins already exist in the blood of the newborn through isoimmunization from the mother, Rh-negative blood should be given whenever possible, reports to the contrary notwithstanding.

Hemorrhage in the newborn period is most frequently accidental and is usually associated with slipped cord ligature and trauma, and the blood lost should be replaced by transfused blood. Stewart Clifford of Boston has expressed the opinion that asphyxial bleeding is of greater importance than either traumatic or accidental factors and that appropriate measures to reduce asphyxial states would decrease the incidence of hemorrhage in the newborn. Prophylactic administration of vitamin K to the mother and infant has practically eliminated the incidence of hemorrhagic disease of the newborn (hypoprothrombinemia neonatorum). Hemophilia is seldom encountered in the newborn period except through surgical intervention or routine circumcision and is also effectively treated by the transfusion of blood. Congenital thrombocytopenic purpura is infrequently seen at this age, and when it is, blood transfusion rather than splenectomy is the treatment of choice, unless the disease cannot be controlled by this procedure. Bleeding from ectopic islands of gastric tissue scattered through the intestinal tract may account for obscure prolonged gastrointestinal bleeding at this period, just as it does in a Meckel's diverticulum.

Infection in the newborn period is often associated with a bacteremia and acute hemolytic anemia or with bleeding and purpura due to platelet depression. Transfusion in addition to chemotherapy is therefore indicated. In my experience and that of others anemia in the newborn that can be attributed to infection is less common in recent years.

A poorly defined entity, which is known as chronic hypoplastic anemia, may occur in the latter part of the neonatal period. It is an anemia of the normocytic type and involves the production of red blood cells without significant changes in white blood cells and platelets. No known cause has been found for this condition. Marrow stimulants have been advocated, but to date blood transfusion is the only satisfactory method of treatment. Splenectomy has been tried in some cases, but the procedure has not had sufficient success to warrant its use as a routine method of treatment.

ANEMIA IN INFANTS (ONE MONTH TO TWO YEARS)

Anemia in infancy is predominantly due to iron deficiency, and the red blood cells become deficient in hemoglobin (hypochromic) and smaller (microcytic) than normal. The obvious primary therapeutic consideration is the correction of the deficiency state by the administration of iron to the infant. On a purely theoretic basis other materials needed for hemoglobin synthesis may be lacking (protein, pigments such as chlorophyl, copper and other trace elements). Inferences drawn from animal experimentation would support such a possibility. Such evidence, however, does not justify the numerous shotgun proprietary preparations that are constantly offered to the profession without clinical facts to support their use. Preparations of this type increase the cost of medical care and minimize the careful evaluation of the cause of the anemia which is so important to well conceived and intelligent treatment.

The clinical evidence for the use of copper in hypochromic microcytic anemias of infants and children is conflicting. It is apparent from experimental work that copper is needed as a catalyst for hemoglobin synthesis and that it is concerned with the utilization of iron. It has not been demonstrated clinically, however, that routine use of copper with iron is necessary or desirable because traces of copper are present in most iron preparations and in the diet. This does not mean that copper is not needed, it merely suggests that routine supplemental use of copper is unnecessary unless the infant has been fed on an exclusive milk diet. In anemia which has proved refractory to treatment with iron in the absence of infection and other conditions which interfere with a favorable therapeutic response to iron, copper deficiency may conceivably be present, and the addition of small amounts of copper (1 cc. per kilogram of body weight of a 0.5 per cent solution of copper sulfate) may be necessary for adequate treatment. This dose should be smaller in older children, and even in young infants smaller doses should be given at first. The indication for such therapy has been minimal in my experience.

The exact status of the whole liver or its water-soluble fraction (Whipple) in the treatment of microcytic hypochromic anemias of children has not been accurately determined. It is possible and reasonable to assume that other nutritional factors necessary for the synthesis of the hemoglobin molecule may at times be deficient and that the deficiency can be corrected by feeding whole liver or its water-soluble fraction. However, this does not call for routine use of expensive liver and iron combinations that are without indication. The indiscriminate use of vitamins in the treatment of iron deficiency anemia beyond that needed for normal nutritional balance is also ill conceived and without sound clinical or experimental evidence. Fifteen to 20 Gm. of puréed liver daily may be given to infants up to 2 years of age, and 30 to 40 Gm. daily to children from the ages of 2 to 6 years.

The therapeutic management of microcytic hypochromic anemia often consists in something more than the correction of a possible deficiency of some substance needed to synthesize the hemoglobin. Insuffi-

cient store of iron combined with increased demand due to a rapid rate of growth, as seen particularly in prematurely born infants, is an important mechanism in the production of iron deficiency. Factors which lead to deficient absorption or excessive loss or which inhibit the utilization of iron are of equal if not greater importance in private practice.

It has been brought out in the discussion that infection and dietary deficiency play a more prominent role in the production of anemias of infancy and childhood than any other factor. This is especially true if such factors are present in the first two years of life. Close to 90 per cent of the anemias seen in pediatric practice are due to infection or dietary deficiency alone or in combination. If vomiting or diarrhea are present, failure of absorption and utilization of materials necessary for the formation of blood are added complications. Deficient iron stores due to maternal anemia during gestation, premature ligation of the umbilical cord at birth and premature and multiple births, together with the factor of increased need for iron due to a rapidly expanding blood volume, hasten the onset of hypochromic anemia and accentuate its severity.

Prophylaxis and treatment of the iron deficiency state should therefore be concerned with something more than administration of a suitable preparation of iron or, failing in this therapeutic venture, recourse to the proprietary shotgun preparations. Attempts should always be made to discover all possible causes for the iron deficiency state. In the adult this is usually chronic loss of blood; in the infant it is more likely dietary deficiency in the presence of increased demand or insufficient reserve, disordered alimentation and infection and frequently two or more of the preceding causes.

Iron therapy has been a controversial subject since its inception. Time does not permit a review of the comprehensive work of Whipple, Heath, Hahn, Wintrobe, Moore and others who have made significant contributions in this field. Moore and his group have conclusively demonstrated that iron is absorbed from the gastrointestinal tract in the soluble or ionized ferrous state. The ionization is facilitated by gastric acid if iron is not too firmly linked with other compounds. The degree to which ferric salts are absorbed depends on the capacity of the gastrointestinal tract to reduce them to the ferrous form. For extemporaneous prescription writing, the use of ferrous salts in acid vehicles would therefore seem to be the most effective type of medication. The following prescription is an example:

Ferrous sulfate	9.0 cc.
Spirit of peppermint	1.0 cc.
Solution of amaranth	1.0 cc.
Syrup of citric acid	60.0 cc.
Simple syrup to make	120.0 cc.

Drams 1 (4 cc.) equals approximately 2.5 grains (0.16 Gm.) anhydrous ferrous sulfate

The use of reducing agents like ascorbic acid or citrus fruits given with iron salts may enhance absorption.

The controversy concerning the relative value of various preparations of iron can be settled practically by stating that since larger doses of ferric salts are necessary than with the ferrous form and since large doses of iron are irritating to the gastrointestinal tract, the practical expedient is to use the preparation less apt to upset the infant or child, other factors being equal. Organic preparations of iron in the ferrous form have been preferred by some for this reason. Ferrous gluconate is an example and is an acceptable preparation. The parenteral use of iron is seldom necessary and is a painful procedure. The amount of iron present in the preparation is no index of its efficacy. It is the amount of iron absorbed and utilized, not the actual iron present, that controls hemoglobin regeneration.

The dosage of iron for therapeutic purposes is subject to wide variations, but the following dosage of ferrous sulfate is effective and is recommended: Birth to 2 years, 4 to 6 grains (0.26 to 0.39 Gm.) daily; 2 to 6 years, 6 to 8 grains (0.39 to 0.52 Gm.) daily, and 6 to 12 years, 10 to 12 grains (0.65 to 0.78 Gm.) daily. Ferric and ammonium citrate is given in daily doses of 2 cc. per kilogram body weight (1 cc. per pound) of a 10 per cent solution. The initial dose of iron should be small, and optimal doses should be approached gradually. The effectiveness of the preparation or adequacy of the dose of iron may be checked by the reticulocyte count just as one does with liver extract or folic acid in pernicious anemia. Within about three days after iron therapy is begun the reticulocytes begin to rise and reach a peak in seven to ten days. The level of hemoglobin and the peak of reticulocytosis is usually in an inverse ratio. The lower the initial hemoglobin value the higher the reticulocyte response which one will obtain with adequate iron medication, and this holds true with the daily increase of hemoglobin in response to treatment. The rate of increase of hemoglobin in response to iron therapy definitely slows as normal values are approached. If a patient with hypochromic microcytic anemia fails to respond after receiving adequate doses of iron and shows no reticulocytic response or disordered alimentation, this is suggestive of infection, chronic inflammation or neoplastic disease. In the absence of these factors, copper, whole liver or its water-soluble fraction may be tried. Such cases are few in number if the patient is on a diet well balanced in protein, mineral-rich foods and vitamins.

Thus far only iron deficiency or microcytic hypochromic anemias have been mentioned, because they are the anemias most prevalent in infants. Dr. Zuelzer has brought out that deficiency states leading to anemia may be produced either because iron and other materials used in the synthesis of hemoglobin are not available to otherwise normal cells or because the cells themselves are abnormal due to deficiency in an essential factor. Pernicious anemia in adults is an example of the latter. True pernicious anemia is rare in children below the age of 12 years. Pernicious-anemia-like macrocytic states of the blood have been observed in infants and children from time to time, in patients with celiac disease, in those with hepatic disease, infection, congenital malformation of the intestine and nutritional deficiency (especially infants fed goat's milk exclusive of other foods). Dr. Zuelzer has recently reported a series of 25 infants with macrocytic anemia, which he proposes tentatively to call megaloblastic anemia. Leukopenia with degenerative changes in the granulocytes and thrombopenia were also present. The syndrome may be produced by a variety of causative agents but always by the same basic mechanism, which is manifested by a characteristic megaloblastic bone marrow. The patients ranged from 2 to 16 months of age, and most of them had infections of the upper part of the respiratory tract or a nutritional

disturbance and deficiency. Therapy with folic acid or liver extract was effective and dramatic with a characteristic reticulocytic response. The megaloblastic pattern in the bone marrow was transformed to normal within a few days. In contrast with pernicious anemia, the deficiency is not on a constitutional basis and once the deficiency is successfully treated relapses do not occur. The oral dose of synthetic folic acid is 5 to 20 mg. daily, the intramuscular 1 to 2 mg., depending on the severity of the case. Where parenteral liver extract is used intramuscularly ½ to 2 units daily of the crude extract is advised, depending on the severity of the case and the reticulocytic response.

Another factor apparently essential to erythropoiesis is vitamin C, or ascorbic acid. Anemia of this type shows its greatest incidence at this age period. Whereas uncomplicated iron deficiencies are microcytic and hypochromic and folic acid deficiencies are usually macrocytic and hyperchromic, anemia associated with uncomplicated scurvy is usually normocytic and normochromic. When complicated by hemorrhage and infection it may reveal iron deficiency, and when it is associated with deficiency in folic acid and other nutritional factors it may be macrocytic in type. The bone marrow pattern in uncomplicated scurvy is normoblastic in type and is not transformed by liver, folic acid or iron unless complicated by factors mentioned previously. Specific therapy with citrus fruit juices or ascorbic acid is necessary for cure and is accompanied by a prompt reticulocytosis. In cases in which iron deficiency or folic acid deficiency accompanies scurvy some response is obtained to treatment with iron or folic acid, but it does not specifically cure the primary cause of the anemia. Some observers feel that the role of ascorbic acid in the production of anemia as a primary mechanism is inconclusive.

ANEMIA IN PRE-SCHOOL CHILDREN (TWO TO SIX YEARS OF AGE)

Anemia occurring during the age period 2 to 6 years is usually due to nutritional deficiency and infection. Infection is a dominant factor and according to Dr. Louis Diamond's figures from Boston Children's Hospital produces anemia in the following roughly estimated groupings: 60 per cent are due to interference by infection with elements necessary for blood building; 30 per cent are due to decreased production of erythrocytes; 9 per cent are due to increased destruction of red cells, and 1 per cent are due to interference with platelet production and a bleeding state.

Anemia on the basis of infection may be of mixed type with microcytosis and macrocytosis at this age period. Such patients respond best to iron and liver therapy after the cause has been removed.

Congenital anemias may have their inception earlier but usually manifest themselves in greatest numbers at this age period. Mediterranean anemia, or Cooley's anemia, is resistant to iron therapy and other forms of treatment, although it is hypochromic in type. The exact nature of this disease is poorly understood, but the best explanation is that it is due to an inborn error of metabolism wherein the marrow cells are unable to utilize iron. Splenectomy has been advised, but it is of little permanent value. The same statement would hold true for the therapy of sickle cell anemia. Congenital hemolytic icterus responds as effectively to splenectomy in this age group as it does in adults.

Because of the predominance of infection at this age period, cases of acute hemolytic anemia or marrow depression due to drugs, particularly the sulfonamide group, are not uncommon, and acquired hemolytic states due to infection, drugs and transfusion reactions occur with increased frequency. An acute form of hemolytic anemia known as Lederer's anemia is difficult to classify on any confirmed etiologic basis but is most effectively treated with blood transfusions. Mention has already been made of the desirability of typing any patient requiring frequent blood transfusion for the Rh factor, since Rh-negative recipients may acquire a sufficient titer of positive Rh agglutinins with repeated injections of Rh-positive blood to have severe hemolytic reactions.

ANEMIA IN SCHOOL CHILDREN (SIX TO TWELVE YEARS OF AGE)

Anemia during the school age period is predominantly due to chronic infection, chronic inflammatory disease or loss of blood. Streptococcic infections and their complications head the list. Pyogenic infection, chronic sinusitis, pneumonia, nephritis, rheumatic fever, tuberculosis and symptomatic purpura are prominent as causes. Under normal conditions the iron reserves are fairly well stabilized at this age and iron deficiency is less common. Effective treatment of the cause of the anemia, together with the institution of a balanced diet, is effective unless the anemia is severe and requires blood transfusions as a palliative measure until the cause can be removed. The constant loss of blood due to the menstrual cycle in girls at puberty together with the growth spurt occurring at that period are basic to the iron deficiency state seen at this time. In the presence of a poorly balanced diet, particularly of iron-containing foods, the degree of anemia may become pronounced. Iron prophylaxis and therapy is important in the management of such cases.

SUMMARY AND CONCLUSIONS

Rational therapy demands a thorough understanding of the physiologic and pathologic factors of the age period in which anemia develops. While deficiency of nutritional substances necessary for the synthesis of hemoglobin and for normal erythropoiesis are important, factors which increase the demand, cause excessive loss or interfere with absorption and utilization of these substances are especially important causes for anemia during the active period of growth. It is for this reason that treatment of anemia in infants and children must be approached from a broad clinical perspective as well as from the point of view of the specific disciplines of hematology.

1819 West Polk Street.

ABSTRACT OF DISCUSSION

ON PAPERS OF DRS. SMITH, ZUELZER, BATY AND PONCHER

DR. M. M. WINTROBE, Salt Lake City: What Dr. Baty had to say concerning the frequency of the various types of anemia emphasizes a significant point. While there has been a great deal of progress in hematology in the past two decades the advancement has been made in the understanding of the less common conditions and the more dramatic ones. Much less has been learned about the most commonly observed type of anemia, that which is associated with infection. In the study of the pathogenesis of such anemia it has been learned that in the presence of infection the plasma iron content is con-

sistently and strikingly low. At the same time, the serum copper is elevated and the amount of free protoporphyrin in the erythrocytes is greater than normal. Pursuing these observations further, it was found that when iron was given by mouth, the plasma iron in patients with infection did not rise at all. However, this flat plasma iron curve is not due to a failure of absorption of iron, for if one gives such persons iron intravenously, one finds that the plasma iron content, unlike that in normal subjects, falls extremely rapidly. It has been possible to show that in the presence of infection there exists some disturbance which leads to the rapid withdrawal of iron from the plasma. If such persons are given radioactive iron the iron is incorporated in the red cells to a much smaller extent than occurs in normal persons. By tracing the distribution of the radioactive iron in the various tissues, it has been found that the greatest proportion is located in the liver. While it is true, as Menkin has reported, that a greater quantity of iron is found in inflamed tissue than in the corresponding normal tissue, the quantity of iron going to inflamed tissue cannot account for the severe drain on iron which occurs in the presence of infection. Investigators are seeking to learn the nature and cause of this disturbance in the metabolism of iron. With regard to the diagnosis of anemia, I would like to make a plea to the physician to acquire the habit of looking at the blood smear of his patient himself. While he will never leave to an assistant the final examination of the heart or some other part of the physical examination, it is strange how even the most painstaking physicians are ready to leave the examination of the blood smear to a technician. Prophylaxis is extremely important in the management of hemolytic disease of the newborn. A life may be saved if one is prepared by having been forewarned through having taken a satisfactory history from the prospective mother and having made subsequent appropriate examinations and preparations. If suitable blood for transfusion is available sufficiently soon, the child's life may be saved. In connection with the pathogenesis of hemolytic disease of the newborn the point may be made again that one must avoid giving blood transfusions indiscriminately and thus running the risk of building up anti-Rh or other agglutinins.

DR. CARL V. MOORE, St. Louis: I should like to add my tribute to that of Dr. Wintrobe to the four men who participated in this symposium. The task of reviewing so broad a subject in the time available was well performed. Dr. Zuelzer correctly emphasized the importance of oxygen tension as a regulator of the rate of red blood cell formation. It is well known that the lowered oxygen tension of high altitudes stimulates erythrocytogenesis. Several years ago it was possible to demonstrate that the reverse is also true: high oxygen tensions depress the red-blood-cell-forming elements in bone marrow. Patients with sickle cell anemia were given high concentrations of oxygen by face mask continuously for twelve days. Regularly, on about the sixth day of oxygen administration, the initially elevated reticulocyte levels began to fall to normal values. Shortly thereafter the red blood cell count also began to decrease; on several occasions, it was a million cells lower by the end of the period than it had been before the administration of oxygen was started. After the mask was removed on the twelfth day, there was a great outpouring of reticulocytes and a subsequent rise in the erythrocyte values. What Dr. Poncher has said about keeping iron therapy pure is extremely appropriate. There is no evidence to indicate that the addition of thiamine, riboflavin or any other vitamin to iron makes the iron more effective therapeutically unless a specific vitamin deficiency coexists. These combinations probably have been developed because physicians are dissatisfied with the effect of iron in the treatment of anemias. Iron is of value, however, only when a patient is deficient in iron; that is, when a hypochromic anemia is present. Under these circumstances it will work by itself. In the other forms of anemia iron deficiency is not a primary factor in pathogenesis and cannot be expected to be corrective, with or without copper and the various vitamins. Diagnosis and appreciation of etiologic factors can be sharpened considerably if use of the shot-gun iron preparations is avoided.

ALLERGIC PERITONITIS

Report of a Case

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Several forms of allergy have been reported in the literature.[1] Among the commoner ones are hay fever, eczema, angioneurotic edema, gastrointestinal allergy, allergic migraine, serum sickness, urogenital allergy, nervous allergy, toxic allergy, drug allergy, allergic headache, bronchial asthma, ophthalmic migraine, some forms of dermatoses and periarteritis nodosa of allergic nature or in association with some other manifestations of allergy.[2] A careful search of our available literature on allergy has not revealed a reported case of allergic peritonitis. Although Harkavy [3] has reported 2 cases of "eosinophilic peritonitis," which our case closely resembles, yet there were present associated involvement of other organs in his cases. In the case here reported the involvement is purely peritoneal. The features, clinical signs and symptoms, laboratory observations and therapeutic responses are so distinctive of allergy that we venture to label this case as allergic peritonitis. Our fortunate discovery of this case may henceforth call attention to one form of allergy which has not been reported heretofore.

REPORT OF CASE

Mrs. V. J. L., aged 31, a married Filipino piano teacher, was admitted for the fifth time to the Philippine General Hospital, with a repetition of the attacks she had had previously.

Previous History.—First Illness: The first attack occurred four years ago, when some two weeks after her first delivery on Jan. 13, 1942 she suddenly experienced severe epigastric pain radiating over the whole abdomen and accompanied with nausea and vomiting, abdominal tenderness and rigidity. The pain was extremely severe; it made her double up, and it occurred in paroxysms at intervals of a few minutes. Blood examination revealed a leukocytosis of 20,000 with predominance of polymorphonuclears and eosinophils (15 per cent). She was, however, only slightly febrile (37.5 C., 99.5 F.). Because of the acute abdominal pain, the tenderness and rigidity over the abdomen (especially noticeable in the right lower quadrant) and the leukocytosis her illness was diagnosed as acute appendicitis, and she was operated on. To the surgeon's surprise, the appendix was normal. It was nevertheless removed. The most noteworthy observation, however, was the presence in the abdominal cavity of an undue amount of amber-colored, slightly turbid fluid, of which 1 liter was removed.

Second Admission: The wound healed normally, but the epigastric pain, nausea and vomiting persisted, increasing in intensity and frequency as the days passed. Associated with

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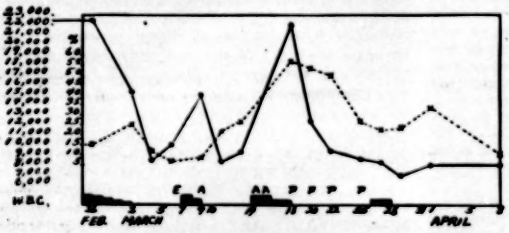
3. Harkavy, J.: Vascular Allergy, Arch. Int. Med. 67:709 (April) 1941.

these symptoms the patient noted a gradual increase in the size of her abdomen sufficient to cause some respiratory embarrassment. After three weeks she had to be readmitted. On this admission blood examination revealed a leukocytosis of 30,000 with 38 per cent eosinophils. A laparotomy was performed and some 3 liters of abdominal fluid was removed. Careful search did not reveal anything abnormal to account for the presence of fluid. Section of the peritoneum revealed no histologic abnormality save for congestion. Examination of the ascitic fluid revealed that it was in the nature of an exudate with high cellular count, high albumin percentage, high specific gravity and high eosinophilic count (38 per cent). Examination of the peripheral blood subsequently revealed a gradual lowering of the leukocyte and eosinophile counts during the next two months until the figures became normal. The laparotomy wound healed uneventfully and the symptoms of pain, nausea and vomiting subsided with the disappearance of the ascites. The disappearance of the clinical signs and symptoms coincided with the gradual return to normalcy of the leukocyte and differential counts. On account of the high eosinophilia, several stool examinations were done for intestinal parasites, but they were consistently negative.

Subsequent Course: On discharge the patient enjoyed comparatively good health and had no complaints whatsoever until after her second delivery in October 1943. The symptoms and signs, which were identical to those of her previous admissions, although less intense, were felt one month after her delivery. In view of our previous experience with her condition she was treated conservatively with sedatives for the pain and regular injections of dextrose and calcium. With this treatment alone she improved. Examinations of blood and of ascitic fluid revealed essentially the same picture as before, and their gradual return to normal kept pace with the clinical improvement. She went home improved and enjoyed good health until July 1944, at which time she was stricken with typhoid fever.



Correlation of hematologic data with abdominal pain and therapy. The unbroken line represents the total white blood cell count; the broken line, the eosinophil percentage; filled in area, abdominal pains; diagonally lined area, menses; A, epinephrine injections; E, estrone, and P, progesterone injections.

Present Illness.—**History:** In October 1945, which was the sixth month of her third pregnancy, she experienced the same symptoms as on her previous admissions. However, the symptoms were felt during and not after pregnancy, as they had been before. The symptoms were comparatively much less in intensity, and the abdominal enlargement seemed only commensurate with the stage of pregnancy. Examination of the blood revealed the same features as before though less in degree. No paracentesis abdominis was done this time. She improved on conservative management within a week.

Her present admission, which is her fifth, followed her last delivery on Jan. 31, 1946 by twenty-six days. The symptoms were first ushered in by epigastric fulness followed by severe pains which radiated downward towards the umbilicus. The pains were severe, paroxysmal and came at intervals of some three to five minutes. They were exacerbated by movements of the body and accompanied by nausea, vomiting of the ingested food and some respiratory distress. The symptoms increased in severity as days passed. Her husband, who is a physician, gave her intravenous injections of dextrose and calcium gluconate, but little relief was obtained. Twice she had to be given morphine for the pain. Gradually, it was also noted by the patient that her abdomen was increasing in size and that the sensation of fulness and bloating was becoming more pronounced. These symptoms did not abate, so she again sought admission. Just before entry, however, she had an extremely acute attack of pain that required morphine to quiet her.

As will be noted all the attacks followed a uniform clinical and laboratory pattern. No jaundice, melena, hematemesis or diarrhea was observed during any of these admissions.

Her condition on admission on February 26 was that of a slightly febrile (37.8 C., 100.04 F.) pale patient under the influence of morphine. She was slightly drowsy and answered questions sluggishly. She still complained of pain, though it was dulled by morphine. Appetite was absent, the bowels constipated, the pulse rate 86, the respiratory rate 20 and the blood pressure 120 systolic and 68 diastolic.

Physical Examination: Physical examination revealed essentially normal conditions except in the abdomen. The abdominal wall was slightly tense and hyperpigmented, with striae of pregnancy. Two scars, that of the appendectomy and that of the laparotomy, were visible. There was evident sagging on both sides. On palpation there was generalized moderate tenderness and rigidity, apparently increased in the right upper quadrant of the abdomen. There were unmistakable signs of ascites.

Previous Diseases: From childhood up to the age of 17 the patient had recurrent attacks of urticaria apparently brought about by the ingestion of sea foods. At the age of 19 she had an attack of moderate epigastric pain and vomiting which was diagnosed as acute gastritis. Examination of the blood done then revealed normal findings. At 21 years of age moderate pallor developed, and she had frequent attacks of dizziness which were diagnosed as due to secondary anemia. She took the contents of a bottle of pills of ferrous carbonate, which relieved her symptoms completely. In December 1939 she had rheumatic polyarthritis which responded to salicylate treatment and extraction of an abscessed tooth. Examination of the blood at this time revealed a white cell count of 12,000 with no eosinophilia. The patient had typhoid fever in July 1944, as stated previously.

Family History: A brother had a history of repeated urticarial attacks. Her father used to suffer from bronchial asthma. Her mother and sister had rheumatic polyarthritis. The results of leukocyte, differential and stool examinations done to these members of her family revealed normal conditions. However, these tests were performed when they were symptom-free.

Laboratory Examinations: Results of examinations of the blood are given in the hematologic studies and on the accompanying chart. Urinalyses were normal on several occasions. The feces were consistently negative for intestinal parasites. Bilirubin tests 1 and 2 and the Takata-Ara test were within normal limits. The cholesterol level was 166 mg. per hundred cubic centimeters. Blood smears for malaria were negative.

The ascitic fluid was light yellow, turbid, rather viscid and slimy. The total cell count was 5,040 with a differential of polymorphonuclears 63 per cent; lymphocytes 7 per cent; mesothelials 1 per cent; endothelials 5 per cent; eosinophils 12 per cent; basophils 2 per cent, and macrocytes, 10 per cent. Guinea pig inoculation of the ascitic fluid was negative, and culture of ascitic fluid was sterile. The sedimentation rate of the blood was normal.

Hematologic Studies: As will be seen in the chart, the white blood cell count ranged from 8,400 to 22,500, the highest count coinciding with the extremely severe pains on admission. During the attacks of pain there was a corresponding rise in the total white cell count.

The eosinophils ranged from 5.5 to 57 per cent. Unlike the behavior of the total cell counts, the increase in the percentage of eosinophils did not correspond with the attacks of pains. However, the eosinophils were observed to present atypical variations during the attacks of pains, as follows: First, the eosinophils were found hard to stain with Wright's, i. e., the granules did not have the crimson red and purple nuclei as seen in the normal smear. The cell seemed larger than

the polymorphonuclear leukocytes when viewed side by side at the center of the smear. There were few vacuolations scattered irregularly around the periphery. The granules were pale pink, more numerous between the lobes of the nucleus and especially affecting those eosinophils with two nuclear lobes. All along the periphery there were scanty granulations, and between the center of the cell and the periphery the granules could almost be counted if there were facilities to do so. The cytoplasm was finely bluish and especially noticeable when there were no granulations.

This atypical appearance of the eosinophils gradually reverted to normal as the clinical signs and symptoms improved, only to be noted again with the return of abdominal pains. The same atypical appearance of the eosinophils was also observed in the ascitic fluid.

Course in the Ward: From admission on Feb. 26, 1946 to March 2, the patient had a low grade fever not above 38 C. (100.4 F.), with associated abdominal pains. Dextrose and calcium were given on alternate days. The pains were not felt from March 3 to 7. Estrone, 1,000 units, was injected at 10 a. m. of March 7, then at 5 a. m. March 8, very severe abdominal pains simulating those felt on admission were observed. Pains were felt subsequently on March 9, 14, 15, 16 and 17. Progesterone was subsequently given, after which no pains were felt. (See chart for better comprehension.)

COMMENT

Salient Features.—The salient features in this case are: (1) the presence of allergy and rheumatic diathesis in some members of the family, (2) the history of repeated attacks of urticaria in the patient, (3) the association of the symptoms with pregnancy and the puerperium (one attack occurred at the sixth month of her second pregnancy and 3 attacks occurred from two to four weeks postpartum), (4) the leukocytosis with eosinophilia during attacks, (5) the syndrome of acute pain in the abdomen during attacks, (6) evidences of ascites during attacks, (7) the intervals of comparative good health, (8) the exudative and eosinophilic character of the ascitic fluid and (9) the apparent absence of a septic focus in the abdominal cavity which could explain the preceding symptoms.

Differential Diagnosis.—In the differential diagnosis we had for consideration the following diseases:

1. Portal cirrhosis was ruled out by normal hepatic function, absence of splenomegaly, the periodicity of symptoms, the absence of evidences of collateral circulation, the exudative and eosinophilic nature of the ascitic fluid and the symptoms of acute abdominal distress.

2. Chronic nephritis was ruled out by the absence of symptoms referable to the urinary tract, normal urinalyses, normal blood pressure, the nature of the ascitic fluid, the periodicity of attacks and the exudative nature of the ascitic fluid.

3. Tuberculous peritonitis was ruled out by the absence of a pulmonary focus, the periodicity of the attacks, the eosinophilic nature of the ascitic fluid, the relative good health of the patient during the intervals and the negative result of guinea pig inoculation with the ascitic fluid.

4. Intestinal parasitism was considered on account of the eosinophilia, but the stool cultures have been consistently negative.

5. Trichinosis was considered because of the decided eosinophilia. Up to the present time no case of trichinosis in a Filipino has ever been reported. Even among the swine no case has yet been discovered by government veterinarians. Clinically, trichinosis can be ruled out by the absence of history of ingestion of raw pork, the absence of symptoms indicative of skeletal involvement, the periodicity of attacks and signs of ascites, which is not found in trichinosis.

6. Periarteritis nodosa [4] was most difficult to exclude, especially if we kept in mind that some cases of periarteritis nodosa are of allergic origin. The acute abdominal symptoms, eosinophilia in the blood and in the ascitic fluid were points in favor of a diagnosis of periarteritis nodosa. Against these were: the periodicity of symptoms; spontaneous remissions; association with pregnancy and the puerperium; absence of involvement of other organs, such as the liver, heart, spleen, kidneys and brain, and absence of evidences of thrombosis, infarction or aneurysm of the mesenteric vessels on laparotomy.

In this regard the report of Harkavy [5] may be mentioned. He described 2 patients with a syndrome of what he termed "eosinophilic peritonitis." These 2 patients (cases 6 and 7) presented, aside from the peritonitis, involvement of other organs such as the liver, lungs and heart, giving a picture of polyserositis of the nature of periarteritis nodosa. In the case herein reported there were no evidences of involvement of any other organ, save for a previous history of urticaria which, however, was apparently independent of the presenting signs and symptoms.

Mechanism of the Ascites.—The possible mechanism of the ascites could not be determined definitely, but we offer the following analysis.

The liver may first be considered. Ascites of hepatic origin may be produced by (*a*) passive congestion, (*b*) portal obstruction or (*c*) periarteritis nodosa with hepatic localization.

Passive congestion was ruled out by the absence of hepatomegaly, cardiac disease, hypoproteinemia or any other condition that may give rise to chronic passive congestion. The exudative and eosinophilic nature of the ascitic fluid, the periodicity and the presence of severe pains were all against this possibility.

Portal obstruction may either be thrombosis or phlebitis. This was ruled out by the absence of splenomegaly, collateral circulation, periodicity of the attacks and the exudative and eosinophilic nature of the ascitic fluid.

The liver as the seat of periarteritis nodosa has been reported.[5] While this possibility may be entertained, yet the periodicity of the attacks, the normal hepatic function, the spontaneous remissions, the association with pregnancy and the puerperium were against such a possibility.

By exclusion, the only logical thing to suspect was the peritoneum, that is, a peritonitis which was proved aseptic by culture and inoculation.

4. Arkin, A.: Clinical and Pathological Study of Periarteritis Nodosa, Am. J. Path. **6**: 401 (July) 1930. Mainzer, F., and Joel, W.: Periarteritis Nodosa as a Manifestation of Sepsis Lenta Due to Streptococcus Viridans, Acta med. Scandinav. **85**: 397, 1935. Friedberg, C. K., and Gross, L.: Periarteritis Nodosa Associated with Rheumatic Heart Disease, Arch. Int. Med. **54**: 170 (Aug.) 1934. Krupp, M. A.: Urinary Sediment in Visceral Angiitis (Periarteritis Nodosa, Lupus Erythematosus, Libman-Sacks "Disease"), ibid. **71**: 54 (Jan.) 1943. Carr, J. G.: Periarteritis Nodosa, M. Clin. North America **13**: 1121 (March) 1930. Scupham, G. W., and Kinney, J. R.: Periarteritis Nodosa, M. Clin. North America, 1945. Kernohan, J. W., and Woltman, H. W.: Periarteritis Nodosa, Proc. Staff Meet., Mayo Clin. **12**: 554 (Sept. 1) 1937. Kerton, I. W., and Bernstein, J. C.: Cutaneous Manifestations of Periarteritis Nodosa, Arch. Dermat. & Syph. **40**: 929 (Dec.) 1939. Harris, A. W.; Lynch, G. W., and O'Hare, J. P.: Periarteritis Nodosa, Arch. Int. Med. **63**: 1163 (June) 1939. Banowitch, M. M.; Polayes, S. W., and Chaul, R.: Periarteritis Nodosa: Report of Five Cases, Ann. Int. Med. **16**: 1149 (June) 1942.

5. McCall, M., and Pennock, J. W.: Periarteritis Nodosa: Our Present Knowledge of the Disease, Ann. Int. Med. **21**: 628 (Oct.) 1944. Pass, I. J.: Infarction of the Liver, Am. J. Path. **11**: 503 (May) 1935. Spiegel, M.: Clinical Aspects of Periarteritis Nodosa, Arch. Int. Med. **58**: 993 (Dec.) 1936. Kountz, W. B.: Periarteritis Nodosa, Arch. Path. **10**: 55 (July) 1930. Klotz, O.: Periarteritis Nodosa, J. M. Research **37**: 1 (Sept.) 1917.

The Allergen.—We are not in a position to define the possible allergen in this case. One outstanding fact, however, is that the symptoms were always associated with pregnancy and the puerperium. Once the symptoms were felt at the sixth month of the third pregnancy and thrice they were felt two to four weeks after delivery. These observations seem to suggest the possible role of the gonadotropic and/or sex hormones in the etiology of the allergy. On account of our lack of facilities to determine blood or urinary gonadotropic or sex hormones, however, we were not in a position to define specifically the role of said hormones in the phenomena observed. In an attempt to ascertain the role of the sex hormones in the etiology of the case we undertook some simple procedures guided only by clinical observations, which fall short in scientific accuracy in such investigations as these.

After a few days, when the patient no longer felt the pain and was resting comfortably, an injection of estrone was given. The resident physician in charge was instructed to administer intradermally 0.1 cc. of the 2,000 unit strength of estrone. Through inadvertence 1 cc. of the medicament was given subcutaneously into the right forearm. After eighteen hours there developed a reaction to the injection, and it consisted of severe abdominal pains similar in character and degree to the pains which the patient had felt on admission. These pains, however, responded dramatically to an injection of 0.5 cc. of a 1 : 1,000 solution of epinephrine. She again had pains of a similar nature on the second, fifth, sixth, seventh and eighth day after receiving the injections of estrone. These pains were alleviated promptly by injections of epinephrine. On the ninth day, we began to give her injections of progesterone every other day for five injections, and since then the abdominal pains have never recurred. Also there was observed a gradual decrease in the size of her abdomen. For purposes of provocation, another injection of 2,000 units of estrone was given after sixty days, and no pain was elicited.

On the site of the first injection of estrone a large erythematous area about 6 by 4 inches (15 by 10 cm.) developed, which discoloration persisted up to the third month's stay. That this local reaction was not due to the solvent of estrone (peanut oil) was demonstrated by the absence of local reaction on the site of the control injection.

Analysis of the Results of These Tests.—With regard to the preceding tests a series of questions may be asked. Was the pain elicited by the injection of estrone causal or casual? If it is causal, why did not the second injection of estrone produce a reaction? Could the second injection of estrone have been so modified or nullified by the preceding injections of progesterone that no reaction supervened?

Or was the lack of progesterone the factor responsible for the phenomena observed in this case, as evidenced by the cessation of pains after progesterone administration? Or was a disturbance of the complicated estrin–progestin metabolism the cause of the allergy? Or were the observations resulting from these tests purely coincidental, as evidenced by the cessation of the pains at about the same time as during previous admissions?

No specific answers can be given. Any attempt on our part to deduce conclusions on such paltry observations will border on mere suppositions without scientific accuracy. However, the preceding observations, coupled with the association of the pain with pregnancy and the puerperium, may warrant the suggestion that the disturbance in the estrin–progestin metabolism was partly if not totally responsible for the allergic manifestations.

SUMMARY

A case of allergic peritonitis is reported. The salient features are: recurrence of symptoms in association with pregnancy and the puerperium; the syndrome of acute abdominal pain during the attacks; the presence of ascites during each attack; eosinophilia in the peripheral blood and in the ascitic fluid; evidences of noninvolvement of other abdominal organs; response of the abdominal pains to the administration of epinephrine; a strong familial and personal history of allergy, and an apparent relationship to the complicated estrin–progestin metabolism.

This case may call attention to one form of allergy heretofore unreported.

BENADRYL IN THE TREATMENT OF CERTAIN DISEASES OF THE SKIN

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In the last year a new drug, beta-dimethyl aminoethyl benzohydryl ether hydrochloride (Benadryl hydrochloride[1]) has become available for clinical investigation and, more recently, for therapeutic use. This compound was prepared by Loew and his associates.[2] It belongs to a distinct pharmacologic group and is believed by its originators to have an antihistamine action. Experimentally, it relieves histamine shock and anaphylactic shock in the guinea pig and exerts an antispasmodic action on smooth muscle. It is a white crystalline powder, soluble in alcohol or water, and can be administered orally or intravenously. We have administered Benadryl to a large group of patients who have had dermatoses characterized by cutaneous edema, such as urticaria,[3] acute or early scleroderma including acrosclerosis and atopic dermatitis. It is the purpose of this report to discuss the results obtained in the treatment of these disturbances with Benadryl and to comment on some of the clinicopharmacologic properties of this drug.

URTICARIA

Urticaria, or "hives," is a condition characterized by localized accumulations of fluid in the skin or mucous membranes. It results from temporary pathologic permeability of blood vessels. Angioneurotic edema or giant urticaria is essentially the same process, except that the subcutaneous tissues are involved and the lesions may occur in the mucosa of the nasopharynx, larynx, bronchi or bladder. Whether the condition is urticaria or angioneurotic edema, whealing is the basic pathologic manifestation.

From the section on dermatology and syphilology, Mayo Clinic.

1. Benadryl was supplied by the manufacturers, Parke, Davis & Company, Detroit 32.
2. Loew, E. R.; Kaiser, M. E., and Moore, V.: Synthetic Benzhydryl Alkamine Ethers Effective in Preventing Fatal Experimental Asthma in Guinea Pigs Exposed to Atomized Histamine, J. Pharmacol. & Exper. Therap. 84: 120-129 (Feb.) 1945.
3. O'Leary, P. A., and Farber, E. M.: Benadryl in the Treatment of Urticaria, Proc. Staff Meet., Mayo Clin. 20: 429-432 (Nov. 14) 1945.

Acute urticaria which follows the injection of a biologic product or the ingestion of food, drugs and the like may last for a few days to a few weeks and usually subsides spontaneously without treatment. When Benadryl is administered, however, relief of the pruritus usually occurs in twenty to sixty minutes, with reduction of the swelling in from two to six hours. We prescribed Benadryl to be taken by mouth every three to four hours in doses varying from 50 to 100 mg. for 35 patients who had acute urticaria. Twenty of these patients were completely relieved in from one to two days; the condition of 12 was improved, meaning that the pruritus receded and that there were fewer, smaller wheals, and 3 patients were not benefited. Side reactions occurred in 10 of the 35 patients but were not severe enough to warrant discontinuance of Benadryl, although this might have become necessary in several instances if recovery from urticaria had not been so prompt.

Chronic urticaria may last for many years; when it does, the cause is more obscure than that of the acute phase of the disease. Patients who have chronic urticaria often are regarded as suffering from fatigue states, although occasional cases are encountered in which illness is the result of visceral disease. The patient who has hives chronically may be wholly or partially incapacitated because of intense itching, insomnia and disfigurement. Wise and Sulzberger [4] have said, that ". . . despite the most thorough 'work-ups' under conditions of the most perfect collaboration . . . most chronic cases [of urticaria] remain unsolved. They run their mysterious course of months or years, often to cease as suddenly and as unexpectedly as they started."

Treatment on the whole has heretofore been ineffective and has consisted of numerous empiric methods. A review of the histories of 75 patients who had chronic urticaria elicited an array of therapeutic agents which they had received or methods with which they had been treated.

Occasionally, some of these forms of treatment have been of curative or palliative value in individual cases, but no single treatment has been of consistent benefit. Moreover, in the evaluation of any remedy for urticaria, study of a large number of patients is necessary, for the condition often subsides spontaneously. The impressive number and variety of treatments which Benadryl replaces are seen in table 1.

With the recent discovery of drugs which possess an antihistamine action,[5] it is now possible to give striking palliative relief to most patients who have chronic urticaria. Of 75 patients treated, 48 were entirely relieved while they were taking Benadryl, 17 had fewer lesions and less pruritus and 10 obtained no benefit. Substitution of placebos or discontinuance of therapy resulted in prompt recurrence of the lesions. Twenty-five patients, or a third of those treated, complained of varying degrees of side reactions to Benadryl, but only 8 of these reactions were of sufficient severity to justify discontinuance of administration of the drug.

The following 2 cases are reported as typical examples of the response of chronic urticaria to Benadryl hydrochloride.

4. Wise, F., and Sulzberger, M. B.: The 1936 Year Book of Dermatology and Syphilology, Chicago, The Year Book Publishers, Inc., 1936, p. 17.
5. Mayer, R. L.; Huttrer, C. P., and Scholz, C. R.: Antihistaminic and Antianaphylactic Activity of Some α-Pyridinoethylenediamines, Science 102: 93-94 (July 27) 1945.

REPORT OF CASES

CASE 1.—A white woman aged 29, a housewife, consulted the section of dermatology of the Mayo Clinic on July 11, 1945 because of generalized urticaria and angioneurotic edema of four months' duration. Lesions occurred during the day or night and often lasted six to fourteen hours. Frequently swellings occurred in the patient's tracheobronchial tree and produced severe dyspnea. Dietary factors were not involved, and results of numerous skin tests had been negative.

Ten minims (0.62 cc.) of epinephrine taken hypodermically gave some relief, but all other forms of treatment, including rigorous elimination diets, sedative agents and the like, had been valueless. For ten months in 1941 the patient had had the same disturbance, but it had ceased spontaneously after dilatation and curettage, which had been carried out because of the increased premenstrual severity of the urticaria. There was no history of infantile eczema, hay fever or asthma in the patient or in her family.

The patient was a well developed and well nourished white woman with multiple pea-sized to palm-sized urticarial wheals asymmetrically distributed over her arms, trunk and thighs. A severe grade of dermographia appeared after the exertion of linear pressure on the skin. Foci of infection were not demonstrated. Results of physical examination and of extensive laboratory studies were not significant.

TABLE 1.—*Therapies Previously Used in Treatment of Seventy-Five Patients Who Had Chronic Urticaria*

Diets			
Milk		Bread and water	
High protein—low sodium		Rowe elimination diet	
Acid ash			
Oral Medicaments			
Arsenic	Ergot	Pilocarpine	Sodium nitrites
Balsam	Fluids	Purgatives	Strychnine
Belladonna	Histaminase	Quinine	Sulfonamide drugs
Bromides	Hydrochloric acid	Salicylates	Thyroid
Calcium	Nitrites	Salt	Turpentine
Emetics	Pancreatic extracts (deinsulinized)	Sedatives	Vitamins
Ephedrine			
Injections		**Procedures**	
Epinephrine		Baths (alkaline, acid, etc.)	
Atropine		Rest cures	
Autohemotherapy		Change of climate	
Desensitization		Psychiatric care	
Hormones		Lotions, salves, etc.	
		Skin tests	
Vaccines			
Escherichia coli			
Streptococcus vaccine			

One hundred milligrams of Benadryl was prescribed for the patient, to be taken three times a day, after each meal. The patient was seen a week later and stated that she had not had hives since taking the drug. She was advised to discontinue the treatment, which she did, but she returned three days later with numerous lesions on her legs, thighs and trunk. With the resumption of therapy she again became free of all urticarial wheals. After the first month of treatment the amount of Benadryl taken was decreased to 150 mg. a day, with equally effective results. Wheals promptly recurred whenever she discontinued the therapy.

This patient had suffered from hives for four months before an effective palliative remedy was prescribed. She must, however, continue to take Benadryl every day, or the lesions will reappear. To the time of this report, she has taken the drug almost every day for ten months, or a total of approximately eight hundred to nine hundred capsules. The cause of the urticaria could not be found.

CASE 2.—A white man aged 20 came to the Mayo Clinic on May 22, 1945 because of severe angioneurotic edema of seven months' duration. He stated that palm-sized swelling occurred almost every day, involving at various times his eyes, lips, tongue, throat, hands, feet and genitals. The lesions were exceedingly pruritic, often painful and lasted several hours to several days. Past treatment, including the taking of epineph-

rine, the use of elimination diets, succinylsulfathiazole and other measures, had been valueless.

Careful interrogation of the patient and the results of extensive laboratory and physical investigations did not reveal a plausible etiologic factor, but fatigue was considered to be a contributing cause.

The patient was given 50 mg. of Benadryl three times a day for two weeks. During this time he was entirely free of angioneurotic edema. On discontinuance of administration of the drug, there was prompt recurrence of the lesions, but when its administration was resumed he once more remained free of lesions for four weeks. He then, on his own volition, discontinued the therapy. When he was seen at the clinic four weeks later, he stated that urticaria had not recurred.

The foregoing case is of interest in respect to two points. First, it indicates that Benadryl gave striking symptomatic relief; second, it illustrates that urticaria may subside spontaneously.

Benadryl has a wide margin of safety and can be taken for many months in succession without deleterious results. It is just as effective in controlling urticaria in the fourth or fifth month of use as it is in the first. The following 10 cases are illustrative of this.

Case 3.—A white man aged 41 had had chronic urticaria and angioneurotic edema for eight months prior to registration at the Mayo Clinic. He now takes 150 mg. of Benadryl a day and to the time of this report has been entirely free of lesions for eight months. Discontinuance of administration of the drug results in prompt recurrence of the urticaria. There have been no unpleasant side reactions.

Case 4.—A white man aged 69 who had had chronic urticaria and angioneurotic edema for two and a half years came to the clinic, where 100 mg. of Benadryl a day was prescribed. He became entirely free of lesions for the first time in two and a half years. Substitution of placebos resulted in the occurrence of new lesions. To the time of this report he has been taking the drug for six months and has not had any side reactions.

Case 5.—A white woman aged 25 had had urticaria and angioneurotic edema for fourteen months. She remained free of hives only so long as she took 100 mg. of Benadryl three times a day, but she became drowsy after she had taken each capsule. After four months of Benadryl therapy she required only 100 to 150 mg. a day and no longer complained of being drowsy.

Case 6.—A white woman aged 26 complained of angioneurotic edema and chronic urticaria of six weeks' duration. Three 50 mg. capsules of Benadryl a day suppressed all lesions but produced dizziness, dilated pupils and dryness of the mouth. To the time of this report she has taken 150 mg. of the drug each day for eight months. She reports that when she does not take Benadryl for a day the lesions recur. She still complains of slight dizziness and dryness of her mouth.

Case 7.—A white man aged 56 came to the clinic because of generalized hives which had occurred daily for thirty years. Innumerable types of therapy had been administered without value. Two hundred milligrams of oral Benadryl each day resulted in complete freedom from urticaria. The patient complained of dryness of his mouth from the capsules. Four 50 mg. capsules controlled the urticaria; three capsules would partially control it, but two capsules would not control it at all. After taking the drug for four weeks, this patient complained of severe drowsiness and was forced to discontinue the medicament.

Case 8.—A white woman aged 29 who had had urticaria for two years complained of dilated pupils and bradycardia which resulted from taking 300 mg. of Benadryl a day. No lesions were present when this dosage was employed. She remained free of symptoms while receiving 150 mg. of the drug a day and had no side reactions. To the time of this report she has taken Benadryl for eight months and requires from one to three 50 mg. capsules a day. Urticaria reappears if she does not take the drug every day.

Case 9.—A white woman aged 59 who had had chronic urticaria and angioneurotic edema of nine months' duration received symptomatic relief from the taking of 150 mg. of Benadryl a day for seven months. No side reactions were present at any time. On one occasion angioneurotic edema of the throat was promptly relieved by the taking of 100 mg. of the drug.

Case 10.—A white man aged 49 who had had urticaria and angioneurotic edema for four months obtained complete relief by taking 150 mg. of Benadryl a day, but he became "jittery" after taking each capsule. To the time of this report he has taken the preparation for five months but still complains of being "jittery" for about one hour after each dose of the drug. Nevertheless, he prefers this reaction to the unpleasantness of urticaria.

Case 11.—A white woman aged 43 complained of hives of three years' duration. She obtained complete relief from the lesions by taking 100 to 250 mg. of Benadryl a day for eight months. No side reactions were observed during this time, and the drug was as effective in aborting or preventing lesions at the end of eight months of therapy as it had been early in the course of treatment.

Case 12.—A white man aged 32 stated that for six and a half years he had had hives and swellings in his throat, which occurred almost every day. One hundred milligrams of Benadryl given four times a day made him dizzy and weak. The dosage was decreased to 50 mg. three times a day, with resultant control of the urticaria. The patient has received the drug for six months, to the time of writing, and has been able to decrease the amount to from 50 to 100 mg. a day. This gives him complete freedom from urticaria. In five months, he has reported, he has had only one attack of hives, and he has not experienced any further side reactions to Benadryl.

ATOPIC DERMATITIS

We used Benadryl in the treatment of atopic dermatitis because of the frequent concomitant occurrence of cutaneous edema, white dermographia, hay fever and asthma in this disturbance.

It is difficult to evaluate our results, because Benadryl seldom was the only remedy prescribed. Patients who have generalized eczematoid changes usually are instructed to take soothing baths and to use wet dressings, antipruritic lotions and similar measures. Benadryl was prescribed as an adjunct to other forms of therapy for 25 patients who had atopic dermatitis. It relieved severe paroxysms of pruritus for 8 of the 25 patients. Patients who have atopic dermatitis frequently experience itching more at night than during the day. Thus, if 100 mg. is taken at bedtime and drowsiness results as a side reaction, it is not an unwelcome reaction. If relief from pruritus is not obtained within the first few days there seems to be little justification for continued use of Benadryl. Aside from the fact that the drug decreased the severity of paroxysms of pruritus for 8 patients, we did not observe any other benefits accruing from its use.

PRURITUS ARISING FROM OTHER CAUSES

Benadryl is not an effective antipruritic drug. It afforded relief to only 6 of 38 patients who suffered from itching due to various causes, such as contact dermatitis, jaundice, toxic pruritus, psoriasis, dermatitis herpetiformis, so-called neurogenic pruritus and the like.

SCLERODERMA AND ACROSCLEROSIS

In the presence of scleroderma and acrosclerosis, edema may be the earliest change seen in the skin. Edema produces stiffness and limitation of motion and may last for varying periods before sclerosis and atrophy occur. Because we were able with Benadryl to decrease or prevent the development of edema in the presence of urticaria, it occurred to one of us (O'Leary) that a similar mechanism might decrease the edema which occurs in scleroderma.

Nine patients who had acrosclerosis and 4 who had scleroderma received Benadryl by mouth in amounts varying from 200 to 800 mg. a day. A chief complaint of the acrosclerotic patients was their inability to flex their fingers or to make a fist. During the first two weeks of therapy 7 of the 9 patients who had acrosclerosis were able, because of the rapid disappearance of edema from their hands, to bend their fingers and to make a fist. Sustained benefit, however, was observed in only 2 of these 9 patients. Of the 2 patients who obtained sustained symptomatic benefit from taking Benadryl, one was a 65 year old woman who complained primarily of stiffness and swelling of her hands. After Benadryl therapy alone, increased mobility of her hands developed, and in a week she was able to flex her fingers. She remained without pain or swelling of her extremities for five months, at the end of which period she discontinued therapy. In a short time the swelling, cyanosis and pain returned, but with the resumption of Benadryl therapy she again gained symptomatic relief. At the date of this report she is still doing well. She has had a total of seven months of treatment.

TABLE 2.—*Side Reactions to Benadryl*

Condition	Patients Treated	Side Reactions
Chronic urticaria	75	25
Acute urticaria	35	10
Atopic dermatitis	25	8
Scleroderma	13	5
Miscellaneous	38	10
Total	186	58 (31 per cent)

The second patient with acrosclerosis who improved definitely was a 24 year old waitress who complained of stiffness and swelling of her face, chest and hands. Small painful ulcers were present on the tips of her fingers. To the time of this report she has received 500 mg. of Benadryl a day for six months. At present the ulcers are healed, the patient is able to make a fist, softening of the skin in the affected areas has ensued, and she is able to work.

TOXICITY

Side reactions of varying degrees developed among 58 of 186 patients (31 per cent) who received Benadryl (table 2). The side reactions in order of frequency were drowsiness, dizziness, weakness and dryness of the mouth. Some patients complained of being "jittery," "on edge," "nervous," "confused," "poorly coordinated," "nauseated" and "excited."

Side reactions usually occur during the first few days after the administration of the drug is begun and frequently diminish in severity or disappear entirely after several weeks of therapy. "Late" side reactions developed among only 10 patients. These occurred for the first time after several months of daily use of the drug. Symptoms of toxicity promptly disappear when the drug no longer is administered. Ten patients were not able to use Benadryl because it apparently caused unusually severe dizziness and drowsiness.

COMMENT

Treatment of urticaria and allied dermatoses should begin with small doses of Benadryl, such as 50 mg. administered three times a day. The amount should be increased gradually until the minimal maintenance dose has been determined. Conversely, patients may require 300 to 400 mg. of the drug a day for several weeks but frequently are able to decrease the amount gradually until smaller doses become equally effective.

Benadryl does not seem to exert a cumulative action, for urticarial lesions promptly reappear when administration of the drug ceases. If relief is not obtained within the first few days, it is unlikely that Benadryl will subsequently be of value, and administration of it should be discontinued. In our ten months' experience with the drug manifestation of cutaneous sensitivity has not been observed, nor is there any evidence to date that it is habit-forming.

Indiscriminate use of Benadryl should be discouraged, for severe side reactions sometimes occur, such as loss of judgment or confusion.

SUMMARY

Benadryl is highly effective in the treatment of acute urticaria, chronic urticaria and angioneurotic edema, but relief is obtained only while the drug is being used. The drug decreases the severity of paroxysms of pruritus for some patients who have atopic dermatitis but is not a potent antipruritic drug. The condition of patients in the edematous phase of scleroderma is temporarily improved; such patients are able, by virtue of suppression of cutaneous edema, to achieve increased mobility in their extremities. Side reactions occurred among 31 per cent of the patients in this study but were severe enough to warrant discontinuance of the administratioin of Benadryl to only 10 patients.

Little Strokes That Go Unrecognized.—In the case of older persons, cerebral arteriosclerosis is perhaps the commonest cause for fatigue and misery and a nervous breakdown. Particularly disabling are the little strokes that so often go unrecognized. Many of them come in the middle of the night. Commonly they are thought to be heart attacks or attacks of Ménière's disease. The gastroenterologist sees many of these patients because so often with the cerebral thrombosis there is a wave of distress which shoots into the abdomen. Often it goes into the thorax, and then the tentative diagnosis may be heart disease. To diagnose the little strokes one must keep thinking of them, and then one may be able to draw forth the typical story of sudden onset and big character change. Often one can get this story only from the family or business associates. Only they will tell of the nervous breakdown, the changes in behavior, the increased irritability, the forgetfulness and the tendency to weeping and depression. The thing to remember is that, with the exception of carcinoma of the pancreas, there is no disease in the abdomen that can quickly change a person's whole character.—Alvarez, Walter C.: What Is the Matter with the Person Who Is Always Tired? *Northwest Medicine*, June 1947.

Clinical Notes, Suggestions and New Instruments

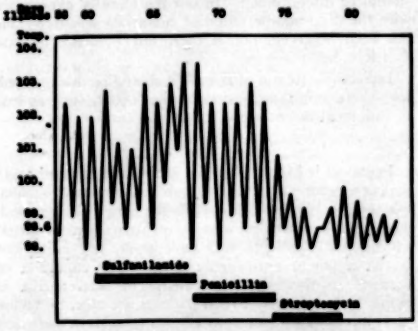
HAVERHILL FEVER DUE TO STREPTOBACILLUS MONILIFORMIS TREATED WITH STREPTOMYCIN

MILFORD H. SPRECHER, M.D.
Elkton, Md.
and
J. R. COPELAND, M.A.
Salisbury, Md.

Haverhill fever, epidemic arthritic erythema, was diagnosed by blood culture in a white man 38 years old, a welder by occupation. Observation began May 25, 1946 and has continued to date. Streptomycin was used by us in the treatment of Haverhill fever for the first time, as far as we are able to determine.

REPORT OF A CASE

History.—B. W., a white man aged 38, while welding in a small compartment of a ship on April 7, 1946, became nauseated, vomited once and had diarrhea for twenty-four hours. He stayed home for two days and then returned to work in spite



The effect of streptomycin on temperature.

of weakness, chills, rises of temperature and night sweats. The temperature established no pattern except to rise in the early evening, and this was not a daily occurrence until May 18, when pain in the legs began.

The pain was intense and was located deeply back of the tibias. It was also present back of the knee joints and in the ankles, yet seemed not to involve all these joints at the same time. Swelling of the joints was not noticeable. In the evenings the patient would first notice the feeling of fever, then in an hour or so the pain in the legs, which continued with sleeplessness until late morning. No rash made its appearance. Cough was present with a little expectoration. The weight dropped to 127 pounds (58 Kg.) from 140 pounds (63 Kg.). Moderate urinary frequency was present without dysuria. The appetite was poor, but eating did not lead to an overfilled sensation. The color of the stool was recalled as brown. There was no shortness of breath or swelling of the feet.

The past history was characterized by an attack of diphtheria at the age of 8, subsequent to which valvular cardiac murmurs were noted. At the age of 27 and again when he was 28 he was treated for cardiac decompensation with rheumatic heart disease. However, vigorous activity was in no way limited until his present illness.

Examination.—Examination on June 4, 1946 showed a man of small stature, who appeared moderately ill and apprehensive. His attitude seemed to be that of seeking immobility, and attention directed to his lower extremities was resented. There was no cutaneous eruption at any place on his body. His right ankle looked swollen but was not red and was without extreme tenderness on pressure. Motion was resented in this joint, as well as deep pressure in the calves. Other joints were free of tenderness, swelling or restriction of motion.

The scalp carried a good coat of hair. The face showed numerous scars from acne. There was slight puffiness of the lower eyelids; the pupils were regular and equal and reacted to light. The conjunctivas showed no jaundice, and the palpebral membranes were light pink. The nasal passages were adequate with only slight exudate. Frontal and maxillary sinuses transilluminated. The teeth appeared good. The tongue was slightly coated, the pharynx was normal and the tonsils were small. The right ear drum was dulled.

The neck was not rigid; the thyroid was not enlarged and the trachea was in the midline. There were many shotlike glands in the posterior triangles.

There were two wartlike linear lesions in the right subclavicular region. The lung fields were resonant throughout and the bases descended in both axillas and in the back. Breath sounds showed no changes. The apex beat of the heart was in the seventh interspace on the left side and was slightly vigorous on palpation. The left border of the heart measured 12 cm. from the midsternum. There was a systolic mitral murmur, rather soft in character, that was transmitted to the left axilla. There was a soft systolic murmur at the aortic area. The peripheral arteries were soft. No definite glands could be felt in either axilla. The pulse rate was 98, the temperature 102.4 F. and the blood pressure 120 systolic and 80 diastolic.

There was slight distention of the abdomen and some rigidity of the rectus muscles. The spleen was not palpable. The left lobe of the liver was enlarged to about three fingerbreadths below the costal margin. This area was slightly tender. Some inguinal glands were enlarged. The prostate and the scrotal contents were normal. Superficial reflexes and the tendon reflexes were present and normal.

Laboratory Examination.—On the initial admission on June 4, examination of the blood revealed that the hemoglobin was 66 per cent, the red blood cell count 4,040,000 and the white blood cell count 10,000, with a normal differential pattern. Examination for malaria was negative. No stippling of the cells was seen. Subsequent examinations on June 15, 20, 21 and 27 showed a progressive anemia, the last blood count being hemoglobin 51 per cent, red blood cells 3,000,000 and white blood cells 13,600. The sedimentation rate was reported as 8 mm. (Wintrobe).

The urinalyses were negative on June 4 and 15 but on June 26 showed 4 plus albumin and 50 white blood cells per high power field. The urine cultures at the time of the pyuria showed Staphylococcus albus and Escherichia coli.

Roentgenograms of the chest revealed normal conditions, and stool examinations were negative. The electrocardiogram was normal. The blood Wassermann test was negative. Blood cultures carried out on June 4, 5 and 6 contained Streptobacillus moniliformis.

Physical signs of chronic rheumatic valvular disease suggested the possibility of endocarditis. Undulant fever was suspected until the positive blood cultures of Streptobacillus moniliformis were reported and the negative agglutination reactions for undulant fever were confirmed.

Investigation by the county health officer brought out the fact that the locker rooms where lunches were kept were overrun with rats.

Bacteriologic Data.—The Streptobacillus moniliformis[1] isolated was first noted as similar to bread crumbs, a growth appearing on the sedimented blood cells of a routine blood culture after six days' incubation. It is extremely likely that

1. Topley, W. W. C., and Wilson, G. S.: The Principles of Bacteriology and Immunity, ed. 2, Baltimore, William Wood & Company, 1936, chap. 13, p. 274.

growth occurred before this time but was overlooked, because in two repeat blood cultures growth was noted on careful observation after forty-eight hours. It was a small, gram-negative bacillary or coccoid organism, rarely producing the filaments that are so characteristic, non-acid-fast and nonhemolytic, which required blood or serum for the maintenance of growth. Growth in serum broth was always from the bottom of the tube and extended up the sides. It was aerobic but was aided in its growth by carbon dioxide. It grew well on chocolate agar and thioglycollate semisolid mediums. It died out rapidly, usually on the third or fourth day in a medium which supported rapid growth. Acid without gas was produced in dextrose and maltose but not in sucrose and lactose. Colonies were discrete, circular and extremely small with raised umbonate centers with crenated edges.

Patient's Agglutination Response to the Organism.—The antigen used was prepared by growing the streptobacillus in serum broth for forty-eight to seventy-two hours, centrifuging at high speed for thirty minutes, decanting, resuspending the sediment in about one third the amount of isotonic sodium chloride solution, killing by subjecting to 52 C. for two hours and diluting to a usable antigen. As stated by Brown and Nunemaker,[2] until the organism has been cultured through fifty or sixty generations it is hard to prepare a homogenous antigen. Since the organism at this time had only passed the twenty-fifth or thirtieth generations it had a tendency to settle after overnight incubation at 52 C. However, it was possible to tell definite agglutination as against settling by resuspending the antigen by shaking. Agglutination tests submitted May 25, May 31 and June 19, 1946 which gave no reaction to Eberthella typhosa O, Salmonella paratyphi B, Brucella abortus, Proteus OX 19 and OX 2 antigens were positive for the Streptobacillus antigen all in the dilution of 1 : 1,280. Several checks were run with negative serums and with serums giving reactions to typhoid and undulant fever antigens, but none agglutinated the Streptobacillus antigen.

Therapy.—While awaiting the report of the blood cultures, sulfanilamide, 0.65 Gm., with sodium bicarbonate, 0.65 Gm., were administered to the patient for seven days. When the Streptobacillus was reported, the administration of penicillin, 30,000 units at three hour intervals was begun and continued for six days. The accompanying chart shows the lack of specificity of penicillin and the dramatic success of streptomycin administered in 0.3 Gm. doses at three hour intervals for five days.

Subsequent Course.—The third dose of streptomycin permanently relieved the pain in the legs, and the temperature remained normal thereafter, except for one day when 100 F. was reached because of pyuria. With the administration of penicillin, the patient's condition had seemed to become more grave.

The liver became more enlarged and decidedly tender on June 22, or about the sixtieth day of the disease, and some fluid seemed to have collected in the patient's abdomen. An albuminuria developed that lasted for another month. It persisted for two weeks after the pyuria had been cleared by the use of sulfathiazole, 0.5 Gm. four times a day.

Cultures of blood taken five days after the administration of streptomycin and again fourteen days later have been negative for any growth.

COMMENT

Haverhill fever is characterized by "an abrupt onset; a rubelliform to morbilliform eruption, chiefly on the extremities, and an inflammation of the joints with marked pain and tenderness." [3] The diagnosis is made by the isolation from blood or from articular fluid of a highly pleomorphic filamentous or spindle-shaped aerobic or microaerophilic gram-negative organism, Haverhillia multiformis, which requires serum for growth in artificial mediums.[4]

Parker and Hudson [5] were responsible for the creation of the name of the organism after study of the cases of Place, Sutton and Willner,[6] who reported in 1926 an epidemic in Haverhill, Mass., of a disease called by them erythema arthriticum epidemicum and Haverhill fever. The organism was the same as that isolated in 1925 by Levaditi and his co-workers [7] from a case of "acute erythema multiformis unassociated with rat bite" and named by them Streptobacillus moniliformis because of its distinctive morphology. Litterer [8] in 1917 obtained an organism from blood cultures of patients with rat bite fever; this he called Streptothrix longus and Streptothrix brevis, and he was the first also to use the term Streptobacillus. Schottmüller,[9] however, in 1914 was the first to describe adequately the Streptothrix which he cultured from the blood of a patient suffering from rat bite fever.

This briefly indicates the confusion attending the organism, when the Streptobacillus moniliformis is described in three languages under three different names and in three different diseases.

It is an apparent normal inhabitant of the nasopharynx of 50 per cent of laboratory rats and of wild rats. It has also been found in pulmonary lesions of rats. It is transmitted through contaminated milk, presumably, and also by the bite of rats. The organism seems to overshadow etiologically Leptospira morsus muris, also known as Spirillum minus, the highly mobile spirillum of uniform morphologic character which causes sodoku,[2] or rat bite fever.

Haverhill fever, as described by Place and Sutton,[3] has arthritis as the most persistent symptom, from the second to the thirteenth day of the disease, subject to remission and recurrences. In addition to definite involvement of the joints there is generalized pain in the legs and arms without local evidence in the joints. Chills usually precede the rash, which was noted in 13 per cent of their cases. Fever is always present, and often there are headache, sore throat and cough. Fever is usually septic, and the temperature returns to normal in one week; but this depends on the degree of articular involvement, and the fever may persist for months.

Treatment of the disease has included use of the sulfonamide compounds and penicillin. The former have been ineffectual, but Altemeier [10] has reported good results with penicillin in cases which were due to the bite of rats and were not Haverhill fever. In experimental animals Heilman and Herrell [11] obtained good results with penicillin. Here again they were dealing with Streptobacillus infections due to the bites of rats.

SUSCEPTIBILITY TESTS

Susceptibility of the Streptobacillus moniliformis to penicillin and streptomycin was carried out by two methods:

Impregnated Filter Paper Method.—No. 1 filter papers were cut into 10 mm. squares, sterilized and wet, in one instance with a solution of penicillin containing 1,000 units, 100 units and 10 units and in the other with a dilute solution of streptomycin. These were dried in a vacuum desiccator over calcium chloride. Serum agar plates were inoculated heavily over the whole surface with a young culture of the Streptobacillus moniliformis and with a young culture of a penicillin-sensitive Staphylococcus aureus. For the penicillin test the different

2. Brown, T. M., and Nunemaker, J. C.: Rat-Bite Fever: Review of American Cases with Reevaluation of Etiology; Report of Cases, Bull. Johns Hopkins Hosp. **70**: 201-327 (March) 1942.

3. Place, E. H., and Sutton, L. E., Jr.: Erythema Arthriticum Epidemicum (Haverhill Fever), Arch. Int. Med. **64**: 639-674 (Nov.) 1939.

4. Farrell, E.; Lordi, G. H., and Vogel, J.: Haverhill Fever: Report of Case with Review of Literature, Arch. Int. Med. **64**: 1-14 (July) 1939.

5. Parker, F., Jr., and Hudson, N. P.: Etiology of Haverhill Fever (Erythema Arthriticum Epidemicum), Am. J. Path. **2**: 357-379 (Sept.) 1926.

6. Place, E. H.; Sutton, L. E., Jr., and Willner, O.: Erythema Arthriticum Epidemicum: Preliminary Report, Boston M. & S. J. **194**: 285-287 (Feb. 18) 1926.

7. Levaditi, C.; Nicolau, S., and Poincloux, P.: Sur le rôle étiologique de Streptobacillus moniliformis (nov. spec.) dans l'érythème polymorphe aigu septicémique, Compt. rend. Acad. d. sc. **180**: 1188-1190, 1925.

8. Litterer, W.: Study of the Streptothrix Isolated in Two Cases of Rat-Bite Fever, Tr. Sect. Path. & Physiol., J. A. M. A., 1917, pp. 275-287.

9. Schottmüller, H.: Zur Aetiologie und Klinik der Bisskrankheit, Dermat. Wchnschr. (supp.) **58**: 77-103, 1914.

10. Altemeier, W. A.; Snyder, H., and Howe, G.: Penicillin Therapy in Rat-Bite Fever, J. A. M. A. **127**: 270-273 (Feb. 3) 1945.

11. Heilman, F. R., and Herrell, W. E.: Penicillin in the Treatment of Experimental Infection with Spirillum Minus and Streptobacillus Moniliformis: Rat-Bite Fever, Proc. Staff Meet., Mayo Clin. **19**: 257-264 (May 17) 1944.

strength papers were spaced across the diameter of the inoculated plates. Since only one strength of impregnated streptomycin paper was used, it was placed in the center of the inoculated plates. Incubation was in a candle can at 36 C., and results were read at forty-eight and seventy-two hours. From the greatest strength of penicillin-impregnated paper the staphylococcus was inhibited for a distance of 15 mm., while the streptobacillus was inhibited for a distance of not over 5 mm. At lower strengths, at which the staphylococcus was inhibited for 12 mm. and 10 mm., the streptobacillus was not inhibited at all. On the streptomycin plate this drug inhibited the growth of staphylococcus for a distance of 10 mm. and that of the streptobacillus for a distance of 17 mm.

Serial Dilution Method.—The medium used was thioglycollate semisolid, which supported a good growth of the streptobacillus at twenty-four hours. Duplicate serial dilutions were made of the two drugs used. One set was inoculated with a

TABLE 1.—*Susceptibility in Vitro to the Action of Penicillin*

Units of Penicillin per Cc. of Medium	Growth: Streptobacillus Moniliformis 24 Hrs.	Streptobacillus Moniliformis 48 Hrs.	Staphylococcus Aureus 24 Hrs.	Staphylococcus Aureus 48 Hrs.
0.8	—	—	—	—
0.4	—	+*	—	—
0.2	+	+	—	—
0.1	+	+	—	—
0.05	+	+	—	—
0.025	+	+	—	+*
0.0125	+	+	—	+*
0.006	+	+	+	+
Control	+	+	+	+

* Growth less than in the control.

TABLE 2.—*Susceptibility in Vitro to the Action of Streptomycin*

Dilution of Streptomycin 1 Cc. Contained 0.1 Mg.	Growth: Streptobacillus Moniliformis 24 Hrs.	Streptobacillus Moniliformis 48 Hrs.	Staphylococcus Aureus 24 Hrs.	Staphylococcus Aureus 48 Hrs.
1:2,500	—	—	—	—
1:5,000	—	—	—	+
1:10,000	—	—	+	+
1:20,000	—	—	+	+
1:40,000	—	—	+	+
1:80,000	—	—	+	+
1:160,000	—	+*	+	+
1:320,000	+	+	+	+
Control	+	+	+	+

* Growth less than in the control

drop of a twenty-four hour growth of the streptobacillus, the other with a drop of a twenty-four hour growth of the staphylococcus. All tubes were incubated in a candle can at 36 C. and the results read at the end of twenty-four hours and again at forty-eight hours. The results obtained can best be seen from tables 1 and 2. Roughly speaking, the streptobacillus is sixteen times more resistant to penicillin and thirty-two times more susceptible to streptomycin than is the staphylococcus. In other words, the organism is decidedly resistant to penicillin and extremely susceptible to streptomycin. In the 3 cases reported by Altemeier and others[10] their results showed a slight difference in the susceptibility to penicillin in vitro of 1 of the 3 streptobacilli isolated. Our results suggest that considerable difference in susceptibility might occur in different strains of this organism, just as they do among the staphylococci. One might venture to say that the difference in results obtained in the treatment of infections caused by Streptobacillus moniliformis with penicillin could be due to the susceptibility or resistance of the strain involved.

CONCLUSION

We would emphasize that: 1. Streptomycin is definitely an effective agent against Haverhill fever. 2. Wild rats can infect food or milk in storage lockers. 3. An alert technician can isolate Streptobacillus moniliformis, though he may not be forewarned of its presence. 4. In vitro tests indicate that the streptobacillus causing Haverhill fever is highly susceptible to streptomycin therapy but resistant to treatment with penicillin.

Council on Physical Medicine

The Council on Physical Medicine has authorized publication of the following report. HOWARD A. CARTER, *Secretary.*

VAN VECHTEN THERMASK ACCEPTABLE

Distributor: Don Parkin Company, 5601 Hollywood Boulevard, Hollywood 28, Calif.

The Van Vechten Thermask provides a means of applying heat to the frontal area of the head and cheeks by controlled electric current. In appearance the appliance resembles a mask, which is attached to the head by means of a ribbon.

The device is constructed as follows: Nichrome wire is wound on a canton flannel base and attached to this base by the addition of a plastic solution (vinyl chloride). This coil is held between two cloth shells, which are also impregnated with the plastic, and the three pieces are joined together by the external application of heat and pressure. The finish is a flock application sprayed onto a urea resin synthetic enamel, making the unit moisture proof with high dielectric properties.

Van Vechten Thermask.

The device was investigated clinically by the Council. This investigation revealed that, for its limited purpose of applying heat to a restricted area, satisfactory results were obtained. This form of applying heat is no more beneficial than the use of an infrared lamp, an electric pad or any other form of applying external heat except that it may be more convenient. The device is useful in furnishing a uniform gentle heat. The Thermask carries the seal of the Underwriters' Laboratories, Inc.

The Council voted to accept the Van Vechten Thermask for inclusion in its list of accepted devices.

ACCEPTANCE OF RADIANT HEATERS

In considering radiant heat generators for inclusion in its list of devices acceptable for use in physical medicine the Council notes that, whereas the so-called "sunlamps"[1] emit a narrow spectral band of ultraviolet radiation of short wavelengths that have a specific biologic action, the radiant heaters of so-called "infrared lamps" emit a wide spectral band of radiation (predominantly of infrared rays) no part of which has a specific biologic action. Moreover, the depth of penetration of these rays into the body is superficial (1 to 10 mm.). Hence these infrared lamps cannot be used as an effective substitute for the diathermy apparatus.

It is further noted that there is no great difference in the spectral quality and the total intensity of the radiation emitted by infrared generators such as bath room heaters and those used in physical therapy. The main differences are the more elaborate adjustable mounting and the more costly finish which, for convenience in operation and for appearance as an office fixture, are incorporated in the professional models.

1. Acceptance of Sunlamps, J. A. M. A. **102**:42 (Jan. 6) 1934; **114**:325 (Jan. 27) 1940.

Two distinct types of infrared generators are available:

TYPE 1.—Tungsten or carbon filaments, heated to high incandescence, in a glass bulb that is mounted at the focus of a concave reflecting mirror; or the filament is inclosed in a conical bulb (of clear or red glass) in which the reflecting mirror is built on the inside of the funnel-shaped part of the glass inclosure. The maximum of spectral energy emitted by the gas-filled tungsten lamp is in the region of 10,000 angstroms. About 30 per cent of the total radiation emitted is of wavelengths that can penetrate deeply (1 to 10 mm.) into the skin.[2]

TYPE 2.—Infrared radiators of the second type consist of an electrically heated solid rod, or a resistance wire (usually of nickel-chromium alloy) embedded in, or wound on, a refractory material, usually porcelain. They are mounted in a concave bowl-shaped reflector and are operated at a red heat, with a maximum of spectral energy emission in the region of 20,000 angstroms to 40,000 angstroms in the infrared (see chart 1 of footnote 2). The bath room heaters in common use are of this type.

In contrast with ultraviolet generators there are no special hazards involved in the use of thermogenic generators (infrared lamps) by the public. The action of infrared radiation is thermal and instantaneous, producing a painful burning sensation if the intensity is too great. Hence there is no excuse for any one getting burned if ordinary care is used.

One of the main considerations involved in the acceptance by the Council of radiant heaters is compliance with the Fire Underwriter's Safety Code; including a wire screen placed over the lamp (in case of breakage) to prevent hot particles falling on the patient if the lamp is suspended over the bed.[3] The high powered (approximately 500 watts or more) infrared generators are intended to be operated at some distance (3 feet or more) from the bed. To reduce the hazard from burns and fire by contact, the reflector should be double walled to prevent overheating. The main fault with many of the infrared heaters is overheating of the porcelain socket that supports the heating unit, with the resultant oxidation of the metal parts and the lead wires at the juncture with the reflector.

The radiant flux (intensity) along with the axis of these lamps varies greatly with the diameter of the reflector, which in turn determines the area that is to be irradiated.

For example, the intensity of a prescription model unit, rated at 220 watts, in a reflector 9 inches in diameter at a distance of 36 inches was practically the same (30,000 to 40,000 microwatts [3] per square centimeter) as that of a 600 watt unit in a reflector 18 inches in diameter; but the area that was uniformly irradiated was much smaller.

In view of the foregoing considerations the Council will accept prescription model units consisting of an infrared radiator mounted on a mechanically stable pedestal stand (adjustable from 3 to 5 feet in height) that permits projection of the beam of radiation in various directions. For use over a bed the infrared lamp shall be provided with a safety wire screen. Furthermore, until a more satisfactory criterion for acceptability of infrared lamps is needed, the Council on Physical Medicine takes into consideration the energy input in the lamp as follows:

In type 1 (glass enclosed tungsten or carbon filaments, heated to high incandescence) the energy input shall not be less than 250 watts.

In type 2 (resistance units heated to a bright red incandescence as described [2]) the energy input shall not be less than 220 watts, preferably 550 watts or greater, depending on the intended use.

In applicator lamps the rated energy input shall be not less than 50 watts, to insure sufficient intensity without making contact with the affected part under irradiation.

In view of the plethora of infrared radiators on the market and the continuing increase in novelties in heating units, it is relevant to note that the Council's acceptance of a device is not to be construed as an aid in sales promotion.

Each new heating device will be considered on its merits.

2. Cahlenta, W. W.: Sources of Ultraviolet and Infrared Radiation Used in Therapy, J. A. M. A. 128: 378 (Oct. 19) 1946.

3. Average summer sunshine is 1 gram calory per minute per square centimeter—70,000 microwatts per square centimeter.

Council on Foods and Nutrition

ACCEPTED FOODS

The following foods which are used primarily for restricted diets have been accepted as conforming to the Rules of the Council on Foods and Nutrition of the American Medical Association.

JAMES R. WILSON, M.D., *Secretary.*

FOODS FOR SPECIAL DIETETIC PURPOSES

The American Dietetic Company, Inc., Yonkers, N. Y.

DIETICIAN BRAND BUTTERSCOTCH FLAVOR PUDDING, containing rice flour, Irish moss extract, salt, artificial flavors, U. S. certified food color, soluble saccharin, dulcin and tricalcium phosphate.

Analysis (submitted by manufacturer).—Moisture 8.0%, ash 9.50%, fat (ether extract) 0.40%, protein (N × 6.25) 5.0%, carbohydrates 60.0%.

Calories.—2.80 per gram; 79.52 per ounce.

DIETICIAN BRAND LOWFAT SALAD DRESSING, containing frozen egg yolks, salt, dulcin, cider vinegar, hydrogenated vegetable oil, water, spice oils and corn starch.

Analysis (submitted by manufacturer).—Moisture 77.40%, fat 12.0%, protein (N × 6.25) 1.0%, total carbohydrates 9.0%, total acidity as acetic acid 0.68%.

Calories.—1.50 per gram; 42.60 per ounce.

PLAN FOR ACCEPTANCE OF JUICES

In order to encourage the production of fruit juices containing high natural levels of vitamin C, the Council accepts orange juice in which at least 40 mg. of ascorbic acid per hundred cubic centimeters of juice is conserved.

The following product meets the standards and rules established by the Council for fruit juices.

JAMES R. WILSON, M.D., *Secretary.*

FRUIT JUICE—ORANGE JUICE

The Cal-Grove Products Company, Los Angeles, Calif.

CAL-GROVE FROZEN-FRESH ORANGE JUICE.

Analysis (submitted by manufacturer).—Soluble solids 13.5%, calories 0.40 to 0.50 per gram, ascorbic acid 43.4 mg. per hundred cubic centimeters.

Council on Pharmacy and Chemistry

NEW AND NONOFFICIAL REMEDIES

The following additional articles have been accepted as conforming to the rules of the Council on Pharmacy and Chemistry of the American Medical Association for admission to New and Nonofficial Remedies. A copy of the rules on which the Council bases its action will be sent on application.

AUSTIN SMITH, M.D., *Secretary.*

MANNITOL HEXANITRATE (See New and Nonofficial Remedies, 1946, p. 336).
The following dosage form has been accepted:
THE NATIONAL DRUG CO., PHILADELPHIA
Tablets Mannitol Hexanitrate: 30 mg.

ASCORBIC ACID (See New and Nonofficial Remedies, 1946, p. 631).
The following additional dosage form has been accepted:
MEAD JOHNSON & CO., EVANSVILLE, IND.
Tablets Ascorbic Acid: 50 mg.

TABLETS BUFFERED PENICILLIN (See THE JOURNAL, March 22, 1947, p. 851).
The following dosage form has been accepted:
E. R. SQUIBB & SONS, NEW YORK
Tablets Sodium Penicillin-G: 50,000 units and 100,000 units with 0.5 Gm. of trisodium citrate as a buffer.

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SATURDAY, JULY 19, 1947

PECULIARITIES OF THE CIRCULATION IN THE LUNGS AND HEART

In a recent Shattuck Lecture Dock [1] states that more progress has been made in the past thirty years in the quantitative study of the circulation of viscera than had been achieved in the previous three centuries. He predicts that the introduction of the vascular catheter and the use of radioactive isotopes will open a vast program of study of the circulation in various organs of normal and diseased men. While much of this advance was made possible by new technical methods, some of the data have been obtained by the injection or perfusion of organs post mortem by a technic that was possible even in the days of Harvey. A description of the circulation of an organ to be complete must include an estimate of oxygen needs, basal and maximal, the capacity of the vascular bed and the volume flow under varying conditions. The rates of flow during life in some organs can now be measured with accuracy.

Because the lungs occupy a large space and blood circulates through them at a relatively low pressure, posture greatly alters the quantity of blood in the apex and base or in the dorsal and ventral parts. Posture also alters the volume flow of blood through the lung. On reclining, the blood that fills the veins below the diaphragm is no longer held back by gravity, and the effective venous pressure, the quantity of blood in the lungs and the output of the heart are increased, the last by as much as 30 per cent in some subjects. Venous blood in the lungs must return to the left ventricle. Because of the effect of gravity on this flow, venous pressure at the bases is 20 to 30 cm. (expressed in its equivalent of water) greater than at the apex of subjects in the orthopneic position. When the patient is in the right semirecumbent posture the venous pressure in the lateral and basal parts of the right lung is 10 to 20 cm. higher than in any part of the left lung. These simple facts are of paramount importance in explaining the frequency of right-sided hydrothorax and of basal pulmonary edema, particularly in cases of cardiac failure. With the rise in venous pressure the flow of lymph also increases, and the removal of bacteria or dusts is most rapid at the base of the lungs. At the apex of the lung, not only is the venous pressure low but the arterial inflow is compromised when adults are sitting or standing. The fall in pressure along the course of the arteries is more definite on the right side because the right pulmonary artery arises at an acute angle from the direction of the flow in the pulmonic conus and pursues a tortuous path around the aorta. Consequently, Dock says, the apical fourth of the left lung and the apical third of the right lung can have practically no blood flow for two thirds of each day in the life of sedentary people. Antibodies formed by the body or antibiotics given parenterally will not reach this zone, and dusts, bacteria and toxins cannot be removed effectively from it when lymph flow ceases. As all this creates ideal conditions for tubercle bacilli, it is not remarkable that tuberculosis flourishes in this region. The high incidence of tuberculosis in congenital pulmonary stenosis, which greatly lowers pulmonic arterial pressure and the low incidence of active tuberculosis in mitral stenosis, with pulmonic pressure several times normal, supports the thesis that arterial inflow is of crucial importance.

The effect of gravity on the lungs thus explains the remarkable efficacy of rest flat in bed in the treatment of apical tuberculosis as contrasted with other types of the disease. Antibiotics will be least effective in reaching apical lesions when patients are allowed to sit up most of the day.

The peculiar relations of the pulmonary circulation to gravity are of great practical effect in the management not only of pulmonary tuberculosis but also of congestive heart failure. While the orthopneic posture makes life tolerable in heart failure it makes recovery impossible in apical tuberculosis.

The human heart probably never uses more than 0.1 cc. per gram of oxygen per minute; during vigorous activity the amount used is believed to be about 0.06 cc., a quantity that can be supplied by a blood flow of 1 cc. per minute. This leaves the venous blood still half saturated with oxygen and with an oxygen tension sufficient to allow diffusion of oxygen into the center of a muscle fiber twice the diameter of those in a greatly hypertrophied heart. Cardiac hypertrophy is a mechanism of great adaptability. In arterial hypertension of gradual evolution the left ventricular wall becomes thicker, but the diastolic capacity does not increase. While the muscular fibers are thicker, they are no longer than normal. However, when increased output must be maintained, as in hyperthyroidism or anemia, the muscle fibers grow longer and the chamber becomes more capacious.

1. Dock, William: The Clinical Significance of Some Peculiarities of the Circulation in the Kidneys, Liver, Lungs and Heart, New England J. Med., May 22, 1947.

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Does the coronary bed adapt itself to the growth of the myocardium? The perfusion of hearts with oil has yielded data on this important question. The coronary perfusibility per gram per tissue decreases as hearts grow from infancy to maturity. Dock found that the flow at ages 66 to 85 was 30 per cent less than at ages 25 to 40. It has been found that in cardiac hypertrophy without coronary disease the blood flow is more than adequate to provide oxygen in excess of the needs of the thickest fibers. The flow per gram also decreases in hypertrophied hearts, but it appears merely as a smooth extension of the curve of the decline in the normally growing heart up to maturity. While the coronary bed adapts itself to the needs of the heart, it is peculiarly liable to atherosclerosis, especially in populations using diets (such as ours) which have a large meat, milk and egg content. Nearly a fifth of the sedentary men of North America die because of vulnerability of the epicardial branches of the coronary system. Even when the aorta and the rest of the arteries are in faultless condition coronary occlusion may occur, particularly in men under 50 years of age. The coronaries at birth have thicker intimal layers than any other vessels of similar size in the body, and this natural thickness of intima increases throughout life. In newborn infants, Dock found that the males had far more striking intimal cushions than the females. This anatomic peculiarity may be the cause of the higher mortality and the earlier onset of coronary disease in males. The predilection of atherosclerosis for the coronary arteries in men and in certain families may therefore be due to an anatomic anomaly present at birth. Fortunately, the adaptability of the coronary circulation under stress imposed by disease is such that normal cardiac function may be maintained for years after the occlusion of the largest arteries in the heart.

VITAMIN A AND BONE GROWTH

Mellanby [1] demonstrated in animal experiments that deficiency of vitamin A in the diet of growing animals causes widespread degeneration of tissue in the nervous system. Of the cranial nerves the olfactory, the optic, the trigeminal and the auditory are reported as especially liable to suffer destructive changes. The dysplasia of bone which resulted from vitamin A deficiency and which was responsible for the grave effects on the nervous system could be largely, if not entirely, explained by altered osteoclastic and osteoblastic activity. The bone changes that result from vitamin A deficiency were demonstrated by Mellanby to be reversible. Soon after the addition of the vitamin the osteoclasts and osteoblasts again become active in their normal positions, the osteoclasts especially being numerous and active, as if making a special effort to remove the superfluous bone laid down or not absorbed in the period of vitamin A deficiency. The bones tend to return to normal.

The dysplasia due to vitamin A deficiency appeared to Mellanby to involve more or less all the bones of the body. Vitamin A, he asserts, plays a controlling part in the molding of all bones. Vitamin A when given in proper amounts insures that bone growth or bone molding proceeds along correct, predestined and safe lines; when the vitamin is deficient, growth continues in an orderly but wrong way, which leads to injury or even destruction of the nervous tissue and ultimately to the death of the animal. The restoration of vitamin A to the diet of the deficient animal quickly brought about a response in the bone cells directed to correct the dysplasia resulting from the absence of the vitamin. Mellanby points out that brain and cord cavities and the foramens which allow the passage of nerves to and from the central nervous system must enlarge to accommodate the growth of the nervous system. If vitamin A is deficient in the growing puppy, bone growth is so changed that the skull cavity and the spinal cord enlarge inadequately and irregularly and the foramens may even become smaller, with destructive results which may include destruction of the olfactory, optic, trigeminal and auditory nerves of the posterior routes of the spinal cord.

Wolbach and his co-workers confirmed in rats the destruction of nervous tissue by bone pressure produced by vitamin A deficient diets, but their interpretation of the cause of the bone pressure differed from that of Mellanby. Wolbach presents evidence [2] which indicates that remodeling sequences attending growth of bone are induced by a factor elaborated in the maturation of epiphysial cartilage cells. He stresses that increase in size of most bones during growth of the skeleton is by endochondral bone formation, for which purpose, until growth is completed, cartilage persists at epidiaphysial junctions. Thus growth of a long bone is accomplished by continuous proliferation of cartilage cells arranged in columns on the epiphysial side and concurrent degeneration of matured cartilage cells on the diaphysial side. The spaces which result from the degeneration and disappearance of the cartilage cells at the diaphysial ends of the columns are penetrated by capillaries accompanied with osteoblasts which are responsible for the deposition of bone matrix on the exposed cartilage matrix. Multiplication, increase in size, maturation and death of cartilage cells are therefore necessary sequences in normal skeletal growth. Preservation of conformation demands continuous remodeling involving resorption of bone where reduction of size is necessary and new deposition of bone from endosteal and periosteal sources to preserve continuity of structure. The deposition of bone by cells of endosteum and periosteum Wolbach

1. Mellanby, Edward: Vitamin A and Bone Growth: The Reversibility of Vitamin A Deficiency Changes, J. Physiol. **105**: 382 (Jan.) 1947.

2. Wolbach, S. B.: Vitamin A Deficiency and Excess in Relation to Skeletal Growth, J. Bone & Joint Surg. **29**: 171 (Jan.) 1947.

refers to as appositional bone formation. In general, endochondral bone formation sets the pace and the pattern of skeletal growth. According to Wolbach, endochondral bone growth in vitamin A deficiency ceases before the growth rate of the animal as a whole is seriously affected. The result of the disproportionate growth of bone and central nervous system is overcrowding of spinal canal and cranial cavity and paralysis resulting from mechanical pressure on brain, spinal cord and nerve routes. Cessation of endochondral growth is not the sole effect of vitamin A deficiency on young bones; remodeling ceases and appositional bone formation continues at different rates in locations which vary with the species but which are in conformity with each normal growth pattern.

Wolbach showed in his experiments that appositional bone formation continued and in certain locations became excessive after endochondral bone formation had ceased in vitamin A deficient animals. Apparently Mellanby and Wolbach agree as to the effect of vitamin A deficiency on bone growth in young animals; but while Mellanby explains this effect by the influence of vitamin A on the activity of osteoblasts and osteoclasts, Wolbach stresses that the effect of vitamin A deficiency is on the epiphysial cartilages and endochondral bone growth.

Current Comment

TOXIC ACTION OF EMETINE HYDROCHLORIDE ON THE HEART

Recently Dack and Moloshok [1] reported 9 cases of amebic dysentery in which toxic cardiac manifestations developed following treatment with emetine hydrochloride. The total doses of emetine varied from 7 to 22 grains (0.45 to 1.42 Gm.). The principal signs of toxic effects on the heart were dyspnea and tachycardia on mild exertion, fatigue and electrocardiographic changes generally involving the T waves. Because of the variation in the dosage of emetine hydrochloride which produced toxic cardiac effects, the investigators believe that there are individual differences in susceptibility to the drug or in the rate of its excretion. Signs of toxic effects were generally apparent in the neuromuscular and gastrointestinal systems before evidence of harm to the heart was manifest. These investigators believe that maintaining the patient at absolute bed rest throughout the course of treatment would decrease the frequency of toxic manifestations from emetine hydrochloride. The pulse rate should be recorded at frequent intervals daily, since tachycardia may be the first clinical sign of toxic effects on the heart. Daily examination and questioning of the patient would help to detect any possible evidence of toxicity, such as fatigue, diarrhea, dyspnea on exertion, muscular tremors or weakness and dizziness. They also advise that an electrocardiogram be taken before treatment is instituted and after administration of the fifth grain of emetine, and that the drug be promptly discontinued if significant changes are found. They believe that in the majority of cases of amebic dysentery the therapeutic effect is as good from the administration of 5 to 7 grains (0.32 to 0.45 Gm.) as with the higher doses sometimes employed. They also recommend that if evidence of amebiasis persists after the first course of treatment—and evidence of toxicity of emetine hydrochloride is not obtained—a rest period of at least a month should intervene before the resumption of treatment. Finally, they say that emetine hydrochloride should not be used in the presence of suspected organic heart disease and should be employed with great caution in patients who are anemic and debilitated.

1. Dack, Simon, and Moloshok, Ralph E.: Cardiac Manifestations of Toxic Action of Emetine Hydrochloride in Amebic Dysentery, Arch. Int. Med. 79: 228 (Feb.) 1947.

EXCERPTA MEDICA AND OTHER ABSTRACT PUBLICATIONS

Excerpta Medica, a new publication with headquarters in Amsterdam, Holland, proposes to provide abstracts in English of every article appearing in every available medical journal in the world. These abstracts are to be issued in the form of fifteen separate sectional journals, each journal devoted to a definite field in clinical or theoretical medicine. This huge task will require some 3,000 specialists all over the world and 400 supervising editors. In each section either one or two volumes will be completed each year and on completion of each volume an index will be included. All published abstracts will bear the signatures of the specialists who prepared them. Abstracts will be numbered in the issues and, to facilitate ready and rapid reference, will be classified in the index both according to the author's name and according to the subject. The first issue offered is section XIII, devoted to dermatology and venereology. The British Medical Association is issuing monthly reports of abstracts in two forms, one dealing with internal medicine and one dealing with surgery, gynecology and obstetrics. It is also understood that Julius Springer Verlag, Berlin, is considering a revival of its zentralblätter and berichte.

PROGRESS IN INTERNATIONAL HEALTH ORGANIZATION

Real progress was made in international organization for health at the International Health Conference [1] held in New York June 19 through July 22, 1946. While all previous international health organizations have been purely informational and advisory in character, the new World Health Organization, under its constitution, will have the right to require certain annual reports from members, as well as to adopt conventions and regulations in specified fields such as sanitation, quarantine, disease, nomenclature, diagnostic standards, biologic products and pharmaceutic products. When the signatures of twenty-six member nations are affixed this constitution will come into force.

1. Masters, Ruth D.: International Organization in the Field of Public Health, advance print of a chapter on public health in the forthcoming Manual of International Organization of the Division of International Law of the Carnegie Endowment for International Peace, Washington, 700 Jackson Place N.W., 1947.

ORGANIZATION SECTION

Medical Economics

MEDICINE AND ECONOMICS

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Current views of the nature and content of what is called economics are as varied and often as bizarre as are some of the plans devised by idealists for the improvement of the human race and the establishment of Utopia. Some are based on misinformation or on partial information, others on prejudice with a minimum of knowledge.

Economics has been defined as a classless scientific study of the means by which people earn their living and of how they spend their income.

Up to a few years ago, few physicians knew or even thought much about questions of supply and demand, of competition, of financial systems, of theories of government. We along with most other citizens went about our businesses or professions, content to live under a democratic government. In spite of its easily recognized faults, it suited us and allowed us the personal freedom and opportunity which we enjoyed, but little appreciated, until we were threatened with their loss.

Now, after a period of war which required sacrifice of life and treasure, regimentation and suffering from the disruption of business and of living necessarily incident to total war, we have added difficulties of class demands and finally proposals that government take over the practice of medicine.

Shall we follow blindly the proposers of theories without consideration of whither they lead, or shall we look into history, where we may find the answers to the same problems in previous decades and centuries? Winston Churchill once remarked "The longer you can look back, the farther you can look forward. This is not a philosophical or political argument —any oculist will tell you this is true."

Much discussion of late has concerned what may be termed the internal economics of medicine: the prospective oversupply of specialists, which, it would seem, we may safely leave to the laws of supply and demand; the overcrowding of hospitals, and the denial of staff appointments to general practitioners in some places. These are faults which can be cured by a liberalization of hospital policies and the adoption of a less selfish attitude by certificants of special boards. The economics of medicine follow the same laws as do general economics, but with the most important modifying influence of the personal relation of physician to his patient.

Medical economics in the larger sense is closely integrated with the general economics of nations. In times of prosperity or of relative political quiet the proposers of revolutionary plans do not find popular support. Periods of stress, resulting from reduction of the opportunity of people to secure adequate food, clothing and other satisfactions of living, prepare the way for the acceptance by the people of theories and procedures of government which sometimes result in desirable reforms but more often bring ruin or delay the accomplishment of remedial measures because they violate economic laws.

The continuing realinements of civilization which we like to think of as advancing, the outcropping of national interests, and revolutions made possible and ultimately produced by the abuses of previous governments have brought into being other forms of government, which may be acceptable or possibly desirable in the countries of their origin but which are repugnant to our own. We here have no wish to dictate the form of government to be established elsewhere, but we do resent attempts from abroad and by malcontents at home to undermine our own democracy with the purpose later to substitute an unacceptable socialist régime. The present proposal to socialize medicine is one step toward this end, directed at medicine because it is vulnerable by reason of defects in distribution and because medical deficiencies are closely related to economic distress.

Some of the advocates of these social changes are sincere in their desire to help the underprivileged but lack the foresight or information, readily available from a study of the economics of history, to appreciate the ultimate results of their well intentioned efforts to aid the downtrodden. They become the ready tools of another group, who use these humanitarian impulses to further a deeper laid plan for the destruction of our form of government. The people are offered a program which promises to give them something they have not had before, whether it be Roman corn or paper money or medical service, and they seize on the new, not considering what they will lose or what the effect will be on their personal liberty or ultimately on their own government.

The unexpected results of new laws are often more significant than those anticipated by the framers of these laws. In our recent labor shortage many men preferred to receive their $20 dole than engage in urgent and legitimate work. In efforts to provide a buffer against adversity in the form of an unemployment dole, men have been encouraged to assume that the world owes them a living. A Negro maid in our community announced that she would take a vacation. Asked why, she said "I like my job, and I get good pay, but I figure that these times won't last and if I don't spend my money I'll have a bad time getting on relief."

We hear now no voices raised in favor of the destruction of food products, the slaughter of little pigs, the plowing under of food crops. Yet only a few years ago the advantages of an economy of scarcity were loudly proclaimed, to a large extent by the same group who would now regiment medicine by governmental edict.

Remarkable is the facility of such people to support unsound measures by fallacious and uneconomic arguments; then when the inexorable laws of supply and demand and the requirements of simple humanity demonstrate their failure quickly they shift to other and equally unsound ground, leaving the wreckage of their previous fiascos for others to clear away as best they can.

Under paternalistic laws more and more is done for people so that their individual responsibility grows less and less and they become finally mere pawns of the state. In order to make such a system operate, dictators are created. There is still retained a figment of representation, but the system operates by compulsion and personal responsibility is lost. Lord Elton, historian and fellow of Queen's College, Oxford, and himself a member of the British Labor Party, in speaking [1] of the relation of England to her colonies in 1770, well said "Later experience has repeatedly shown that representation without responsibility is the most dangerous of halfway houses to democracy."

COMMUNISM IN THE COLONY OF VIRGINIA

A communal system is no stranger in this country. It was tried and failed under John Smith in the colony of Virginia. Its operation is described in a report of Sir Thomas Dale, successor to Capt. John Smith, to the British Crown, quoted by Lord Elton.

"The early colonists had labored under two crippling disadvantages, communal ownership and its inevitable consequence, martial law. . . . The business of all proved to be the business of none." Men would not work for the common store as they would have worked for their own families, and Smith and his immediate successors had to drive their reluctant fellows with savage threats and punishments.

Condensed from an address delivered to the Columbia Medical Society, Columbia, S. C., April 14, 1947.

1. Lord Elton: Imperial Commonwealth, New York, Regnal and Hitchcock, 1946.

"The effects of a very partial introduction of private property under Sir Francis Dale were startling and immediate. Each man was given 3 acres of his own but still had to work eleven months out of twelve for the general store. Even so the lazy became industrious overnight.

"When our people were fed out of the common store and laboured jointly together, glad was he who could slip from his labour or slumber over his taske; he cared not how, nay, the most honest among them would hardly take so much true paines in a weeke, as now for themselves they will doe in a day; neither cared they for the increase, presuming, howsoever the harvest prospered, the general store must maintaine them, so that wee reaped not so much Corne from the labours of thirtie as now three or foure doe provide for themselves. . . .

"Gradually but only gradually the authorities in England came to realize that communal ownership and compulsion must go hand in hand. . . ."

EFFECT ON QUALITY OF SERVICE

That socialized medicine interferes with the physician-patient relationship is self evident by the recognition of advocates of socialized medicine of the necessity of providing a panel. The most shrewd advocates of socialized medicine have failed utterly in their contention that their plan will not interfere in this fundamental confidential relation of doctor to patient. It always has and always will. Indeed, this interference is part of their plan, although the more ardent advocates will not admit it.

The delegation of dictatorial power to one man, even though he may be advised by a council appointed by the same authority, is urged because, it is stated, there will be a tremendous amount of detail to be handled. This is true, and it will require also an enormous addition to our already swollen army of civil servants, much greater than was required for temporary wartime control of production and prices.

Physicians have up to now been individualists; they do their best work on a competitive basis. If the physician is alert, well trained, honest, proud of his profession and its achievements, he will strive continually to improve and give better service, and he is rewarded by the gratitude of his patients and in increase in his clientele and emoluments. To the degree that he is poorly prepared, slothful and loses his incentive to improve, he will do less creditable work. He will be limited by the deadly average of attainment, loss of initiative and dependence on a paternal government, which has always been the next step downward in socialistic governments of history. The removal of the individual incentive is fatal to progress, and human nature is the same, irrespective of occupation. Socialized medicine will reduce the quality of public service as it has in modern governments elsewhere.

Many social injustices and inequalities remain to be corrected. These become more evident as our general standard of living rises from decade to decade, but the remedying of these faults should not be made the occasion for destruction of past gains. In medicine, inadequacies in medical care are closely interlocked with general economic deficiencies. Understaffed and economically poor communities and areas require individualization of treatment, and a plan which will be efficient in one region may not work in another with a different local ideology and economy.

EFFECTS ON DEMOCRACY

While these effects on medical service to the people are serious enough, the less obvious and temporarily more remote effects of a program of socialized medicine on our government are a still greater threat to our national welfare.

A national plan by which government would take over the practice of medicine implies uniformity and loss of personal initiative. Uniformity, whether it concerns the administration of full medical care or of full employment, invokes the sovereign power of the state. Invoking these inherent powers of government to change this and that can lead only to the destruction of democracy and of personal liberty and free enterprise and to the institution of a dictatorship. This inevitable result has come to governments throughout all history from Greece, Rome, Florence down to postrevolutionary France and Nazi Germany. But it is argued that the present plans for government controlled medicine do not envisage any sweeping attack on democracy. At the same time it is averred that an extensive system of bureaucratic control will be necessary to make the program effective. The establishment of such uniform control would be a long step toward authoritarianism more certain in its effect than the legalization of the first issue of paper securities by the French Assembly in 1789.

UNIFORMITY—GOOD OR BAD

Uniformity of itself is not good nor is it bad, considered apart from its effects in the special field in which it is applied. There are many fields of community and national life in which uniformity of action is economically necessary, and these have resulted from science and invention; they are part of what we call the advance of civilization and permit the rise in standards of living. Mass production and the division of labor with the aid of machinery have made possible the enjoyment of comforts and shortened the hours of labor. Most householders do not maintain their own supplies of gas or electricity; if, however, such facilities are not available, they may still light their houses with kerosene lamps or candles. In recent years the gas cylinder and the local air or gas power plant have brought these conveniences to rural areas. The problems of supply of raw materials and of expense vary in different communities according to availability of fuel and the exigencies of climate, and so uniformity is limited by practical considerations. At the same time the householder is under no compulsion to employ them unless he so wishes.

In medicine, rules such as those for quarantine to prevent the spread of disease, for the handling and dispensing of food supplies, for dealing with epidemics have been found by experience necessary in order to do for the individual what he cannot do for himself, and for this purpose local, state and national health departments have been created. In all these, methods have been devised to deal with populations *en masse* for the prevention of disease, and uniformity of method is necessary for their accomplishment.

In education it is recognized that illiteracy is a threat to the life of the state. The welfare of the nation is best served by a system of public schools which can be maintained only by general taxation, under laws administered by the individual states of the Union. The problem of education is general; that of illness is individual. Some states are less able economically than others to maintain current standards and need help, but this need whether educational or medical must not be made the occasion for an invasion of the rights of states by federal bureaucracies.

Uniformity is thus good so long as it makes possible the attainment of desirable ends. Even here uniformity might be bad if it attempted to make all procedures for public utilities the same without regard to climate, natural resources or qualities of populations and also failed to consider that the economic requirements, financial status and abilities of a population today may be different tomorrow. From the beginnings of our government in the early colonies, diversity to meet local conditions and wishes of the citizens has been the rule, rather than uniformity. In the words of Woodrow Wilson, "There was no invariable pattern but everywhere on the contrary a spontaneous adjustment of political means to place and circumstance."

Uniformity provided by a national law for government practice of medicine would not correct the deficiencies in needy areas whose problems require varying treatment: at the same time it would impose an inferior quality of service on all.

MONOPOLIES

The institution of a government monopoly of medical care will produce the same results as have monopolies of the essentials of life in the past, whether it be the accumulation of grain by an Egyptian pharaoh or the acquirement of lands and vast sources of wealth by a Roman tyrant or the monopoly of business by Louis XIV. We have already seen in our own national life the ill effects of great business monopolies: the Sherman Antitrust Act was passed to prevent the stifling of competition. Monopoly of labor through unions originally designed to obtain justice and fair treatment for labor has now

resulted in profit to a few of one class, to the detriment of a still larger class of labor, by denying them free opportunity to work. Monopolies whether of capital or of labor work to the benefit of their sponsors only so long as they are exceptional—when they become general they are destructive of the general welfare and ultimately destroy their creators. For this reason socialists and communists favor monopolies in business and in medicine as factors forwarding their own objectives.

Governmental monopoly of any product results in governmental dispensing of that product to its subjects. The recipients of government largesse look more and more to the government and, like the early colonists of Virginia, work less and less and invite the compulsion which precedes socialistic slavery and ultimate dictatorship.

The seriousness of some economic thinking in our own time was summarized in a recent political utterance ascribed to a counselor now dead and startling in its unashamed frankness: "We shall spend and spend, and tax and tax, and elect and elect."

Care of people by a paternalistic government results in loss of their sense of personal responsibility, first to participate in government, and later to make any effort to contribute to the general welfare.

In urging the theory of the right of a citizen to be cared for, social workers, betrayed by their own idealism, forget that this citizen has also an obligation in a democracy himself to contribute to the general welfare. Without insistence on this obligation, democracy fails.

We are just now emerging from a period of governmental regulation and centralization under bureaucracies made necessary by total war. This period, in which we have become somewhat inured to regimentation, is especially dangerous to our democracy. Socialist and totalitarian governments grow by steps, slowly at first, but with a steadily increasing tempo and always by deluding the people into the belief that the new will be better than what they already have. Government monopoly whether in business or in medicine inevitably leads to the abuse of power and deterioration of quality of service.

Governmental regimentation of medicine would give the American people an inferior rather than a better quality of medical service. What is even more vital, such regimentation would be another long step toward the destruction of free enterprise and of American democracy. As we love our country we shall exert our every effort as individually responsible citizens to maintain the freedoms which are characteristic of America, and the liberty that makes our country the land of the free, the home of free enterprise and of opportunity.

122 South Michigan Avenue.

Coming Medical Meetings

Alaska Territorial Medical Association, Fairbanks, July 28-30. Dr. William J. Blanton, Juneau, Secretary.

American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Hot Springs, Va., The Homestead, Sept. 4-6. Dr. James R. Bloss, 418 Eleventh St., Huntington 1, W. Va., Secretary.

American College of Surgeons, New York, Waldorf-Astoria Hotel, Sept. 8-12. Dr. Paul B. Magnuson, 40 E. Erie St., Chicago 11, Secretary.

American Congress of Physical Medicine, Minneapolis, Hotel Radisson, Sept. 2-6. Dr. Richard Kovacs, 2 E. 88th St., New York 28, Secretary.

American Congress on Obstetrics and Gynecology, St. Louis, Municipal Auditorium, Sept. 8-12. Mr. Karl S. Richardson, 24 West Ohio St., Chicago, Business Manager.

National Medical Association, Los Angeles, Aug. 18-22. Dr. John T. Givens, 1108 Church Street, Norfolk 10, Va., Secretary.

Nevada State Medical Association, Reno, Sept. 4-6. Dr. Moreton J. Thorpe, 17 N. Virginia St., Reno, Secretary.

Oregon State Medical Society, Portland, Sept. 4-6. Dr. Thomas S. Saunders, 1020 S. W. Taylor St., Portland 5, Secretary.

Southeastern Dermatological Association, Knoxville, Tenn., Hotel Andrew Johnson, Aug. 31. Dr. A. H. Lancaster, 608 W. Main Ave., Knoxville, Secretary.

Utah State Medical Association, Salt Lake City, Sept. 11-13. Dr. Ray T. Woolsey, 610 McIntyre Bldg., Salt Lake City 1, Secretary.

Washington Letter

(From a Special Correspondent)

July 16, 1947.

Sanitation Survey by U. S. Public Health Service

The U. S. Public Health Service has reported that a minimum expenditure of $7,834,581,000 is required to improve American water supplies and waste disposal facilities to protect the public from filth borne diseases. Sanitary engineering division of the department bases the estimate on a national survey described as "the most complete inventory of basic sanitary needs ever compiled for the nation." This figure was described as the minimum required to reduce incidence or potential incidence of such diseases as dysentery, diarrhea and typhoid. Surg. Gen. Thomas Parran's comment is that "a sanitary environment for every one is a basic requirement of a national health program." The report stated that waterworks construction, sewage facilities, rural sanitation and garbage collection were required.

Latin American Pediatricians Attend Three Day Congress

A delegation of 414 Latin American pediatricians and several hundred American doctors attended the three day Pan American Congress of the American Academy of Pediatricians. The congress was organized to give Latin American pediatricians an opportunity to consult with the academy's United States membership. Three American doctors were made honorary members of the Latin American division of the American Academy: Joseph S. Wall, Washington, D. C., Henry F. Helmholtz, Mayo Clinic, and Clifford Grulee, Evanston, Ill. Drs. Grulee and Wall also received the Carlos Finlay award for promoting intercontinental advance of pediatrics.

Dr. Parran Prefers Murray Bill to Taft Health Measure

Surg. Gen. Thomas Parran of the U. S. Public Health Service said in a statement prepared for a Senate Public Welfare subcommittee meeting that the health service prefers the Murray Health Insurance bill to that submitted by Senator Taft. The Murray bill would set up a national system of compulsory health insurance to finance medical services for some 85 per cent of the population through a pay roll tax. The Taft bill asks Congress to provide 200 million dollars annually for each of five years to aid states in setting up medical care programs for low income families. Edward F. Poss, Toledo, speaking for the Fraternal Order of Eagles, testified that the Taft bill was "a forward stride in solving some of the health problems," whereas Dr. Allan M. Butler, professor of pediatrics, Harvard Medical School, advocated the Wagner-Dingell bill.

Committees Agree on Federal Cancer Research Fund

House and Senate conferees tentatively agreed on the 1¼ billion dollar appropriation bill of the Labor Department's Federal Security Agency for 1948. The measure includes $14,000,000 in federal aid for cancer research and would also allot funds for research on streptomycin. The House had originally approved $17,328,000 for both programs, and the Senate reduced this to $12,000,000.

Doctors Can Go to Canal Zone to Study Malaria

Medical personnel of the District National Guard who want the training can take a twelve week course in malariology at Fort Clayton, Panama Canal Zone. Special courses in various phases of military medicine can be taken at the Army Medical Center in Washington and at army hospitals and medical centers at Denver, Atterbury, Ind., and Fort Sam Houston, Texas.

Health Precautions Planned for Bikini Resurvey

Capt. Christian L. Engleman, U. S. Navy, will serve as project officer under Capt. Thomas H. Hederman, U. S. Navy, who will command a scientific resurvey of Bikini atoll this summer to determine long range effects of atomic bomb tests made there last year. Captain Engleman will coordinate radiologic health and safety plans.

Bureau of Information

LOCATION OF PHYSICIANS

Virginia Shuler
Chicago

This is the fifth of a series of charts showing the trend in locations of physicians from April 1946 to January 1947.

"The distribution of physicians in New Jersey is quite satisfactory. There is no appreciable shortage of physicians in any rural county. There is little evidence of migration of physicians, at least from within the state. The difference in figures pertaining to physician population 1946 and 1947 does not represent migration but rather the return of physicians from military service, most of whom returned to their original location. There has been a moderate increase in physician population in our urban areas. The physician population in rural counties is now at its prewar level, with no appreciable increase.

"New Jersey is a compact, industrial state. We do have what we consider rural counties, but they are not the type of rural counties contained within many other states. Our farms are mostly of the small, family type farm, not the large farms common in Western states, and all are located within a reasonable distance of centers of population. For these reasons the rural health problem is not a major problem in New Jersey.

"Our chief hospital need is facilities for the care of the chronically ill. This need is in no way due to lack of appreciation of responsibility or obligation on the part of the profession but to the lack of appropriations to cover the cost of such institutions. We have one county, a rural county, Hunterdon, without a voluntary general hospital. For several years there has been a trust fund available in this county for the construction of a hospital, but at present the population of the county does not feel that a hospital is necessary. They are accommodated in the hospitals of surrounding counties, namely Warren, Somerset and Mercer. There is one point in the county which is 20 miles from a general hospital, the greatest distance of any point in the state from a general hospital.

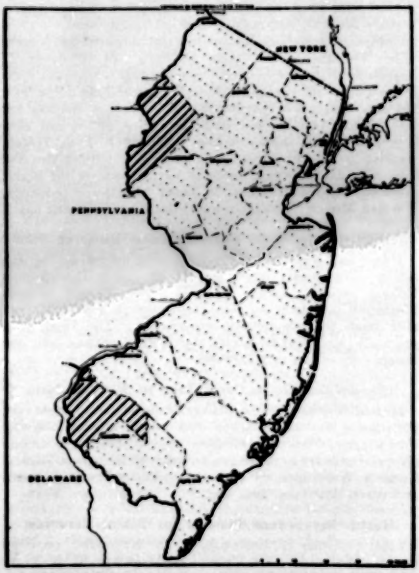
"A plan for state financial aid to our municipalities is available through New Jersey Municipal Aid Administration to all municipalities in the state for medical care of the indigent. Participating municipalities under this plan at present represent 90 per cent of the state's population. The only large municipality not accepting state aid but handling the problem entirely at its own expense is the city of Hoboken.

"In addition, at a state level, are the following agencies providing categorical assistance including medical care: the New Jersey Commission for the Blind, the New Jersey Crippled Children's Commission, the New Jersey State Board of Children's Guardians, the New Jersey Rehabilitation Commission, New Jersey Old Age Assistance Commission and New Jersey Workmen's Compensation Commission. Through the state department of health are operated Baby Keep Well Stations and Venereal Clinics in each large municipality.

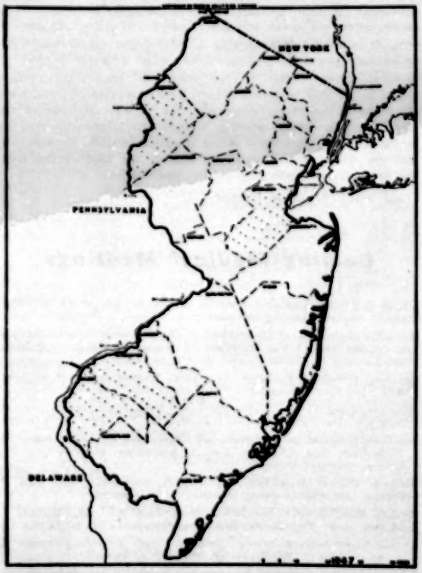
"Over 900,000 persons are enrolled in Hospital Service Plan of New Jersey, the New Jersey Blue Cross Plan, serving employed groups in every county throughout the state, with the cooperation of two hundred hospitals under contract with the plan as cooperating hospitals. Over 90,000 persons are enrolled in Medical-Surgical Plan of New Jersey, the nonprofit prepayment plan organized by the Medical Society of New Jersey, serving employed groups throughout the state with the cooperation of over 3,400 participating physicians."

Norman M. Scott, M.D., Executive Assistant,
Medical Society of New Jersey,
31 Clinton Street, Newark 2, N. J.

NEW JERSEY—1946



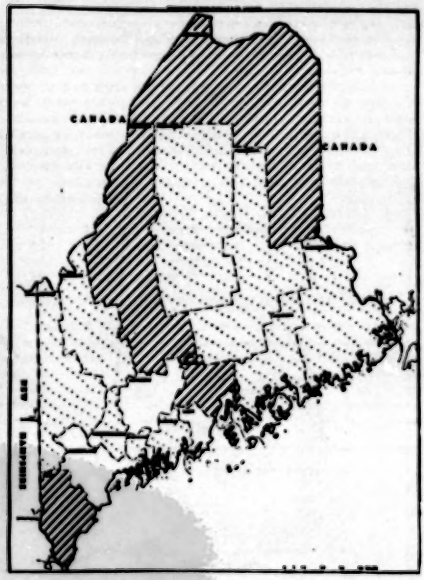
NEW JERSEY—1947



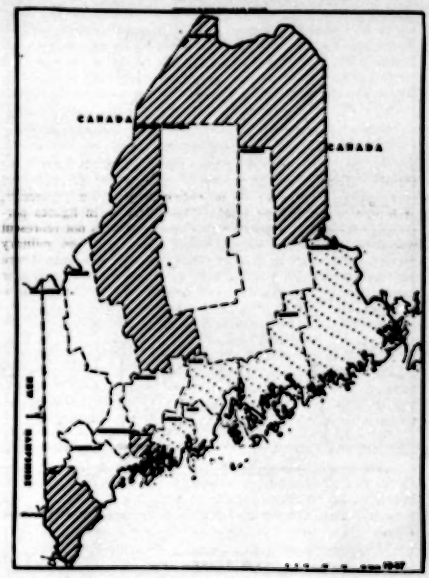
Population, based on 1943 estimated Census figures, per active physician (excludes teaching, research, hospital administration, public health and state hospitals) by county.
Key: Physician-population ratio by county: plain area 1-999, dotted area 1,000-1,499, striped area 1,500-2,999, checked area 3,000 and over, solid black area no doctor.

No areas in New Jersey requesting general practitioners.

MAINE—1946



MAINE—1947



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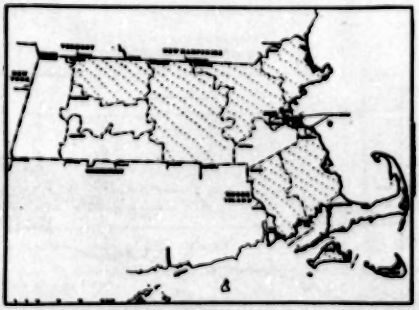
Key: Physician-population ratio by county: plain area 1-999, dotted area 1,000-1,499, striped area 1,500-2,999, checked area 3,000 and over, solid black area no doctor.

Area in Maine Requesting General Practitioner

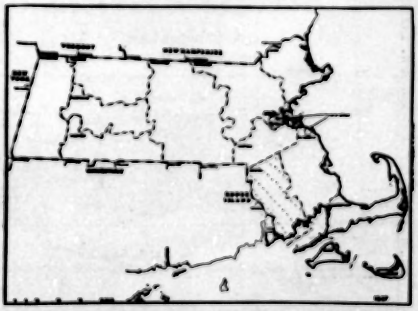
County	Town	Population
York	Cornish	529

MR. W. MAYO PAYSON, Executive Secretary,
Maine Medical Association,
142 High Street, Portland 3, Maine.

MASSACHUSETTS—1946



MASSACHUSETTS—1947



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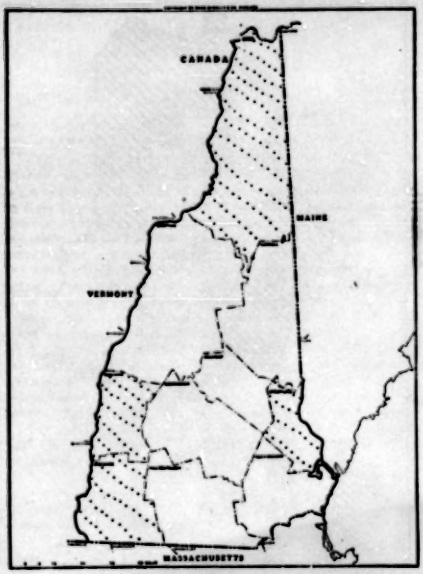
Key: Physician-population ratio by county: plain area 1-999, dotted area 1,000-1,499, striped area 1,500-2,999, checked area 3,000 and over, solid black area no doctor.

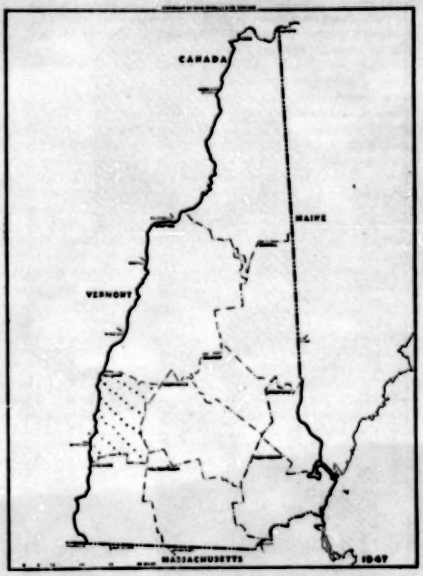
No areas in Massachusetts requesting general practitioners.

JOSEPH GARLAND, M.D., Secretary,
Massachusetts Medical Society,
8 Fenway, Boston 15.

NEW HAMPSHIRE—1946



NEW HAMPSHIRE—1947



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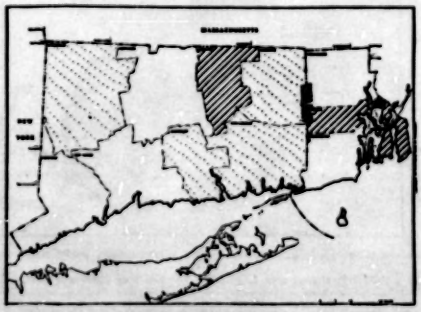
Key: Physician-population ratio by county: plain area 1-999, dotted area 1,000-1,499, striped area 1,500-2,999, checked area 3,000 and over, solid black area no doctor.

Areas in New Hampshire Requesting General Practitioners

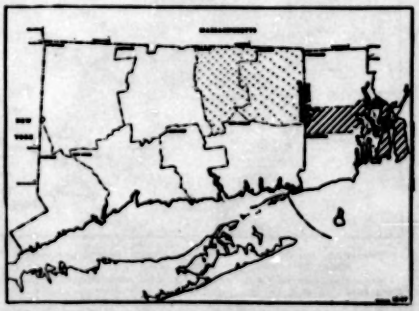
County	Town	Population
Cheshire	Marlboro	1,855
Grafton	Lisbon	1,197
Rockingham		88,142
Strafford	Durham	938
Sullivan	Plainfield	125
	South Acworth	150

C. R. Metcalf, M.D., Secretary,
New Hampshire Medical Society,
5 South State Street, Concord, N. H.

CONNECTICUT—1946
RHODE ISLAND—1946



CONNECTICUT—1947
RHODE ISLAND—1947



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Key: Physician-population ratio by county: plain area 1-999, dotted area 1,000-1,499, striped area 1,500-2,999, checked area 3,000 and over, solid black area no doctor.

No Areas in Connecticut requesting general practitioners.

"This state has more physicians than before the war and a slightly increased estimated population. There was a large in-migration of physicians in the months just after military demobilization, and this continues in a lessened degree. The greater proportion of these in-migrants were veterans who had practiced in the metropolitan New York area before the war. A few physicians can still be located in this state but only in carefully selected areas. There are many openings in full time public employment, no part time. Specialists in pediatrics, obstetrics, ophthalmology and otolaryngology, American board diplomates or equivalent, can be considered and some rural openings are apparent."

CREIGHTON BARKER, M.D., Secretary,
The Connecticut State Medical Society,
258 Church Street, New Haven 10, Conn.

No areas in Rhode Island requesting general practitioners.

"Because of its geography, Rhode Island is ideally equipped to provide adequate medical care and facilities conveniently to all its residents. No resident is beyond 15 miles from a hospital, and with paved roads crisscrossing the area, transportation is swift and convenient.

"The physician population, as in every state, centers about the large cities. As Rhode Island is better than 92 per cent urban, the situation is ideal. There is no appreciable rural health problem, as physicians can easily move into the limited rural districts from the urban centers or have patients brought to the cities.

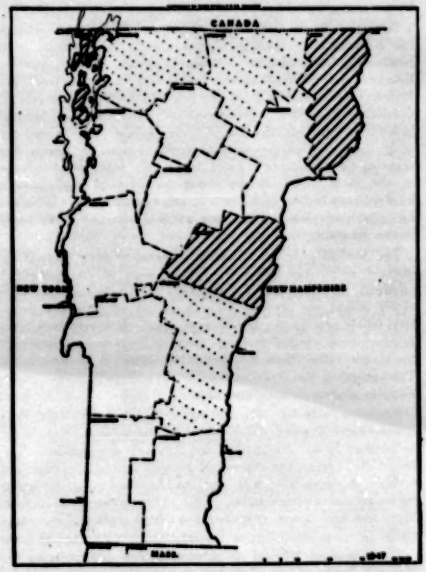
"There has been little migration of the physician population due to the war. A few physicians have settled in other states, but their loss has been more than compensated by the arrival here of many young men returned from the armed forces plus several men moving to Rhode Island from other states.

"Successful financial programs have been completed for additional hospital facilities which include the construction of a five million dollar new Rhode Island Hospital. Plans are under way for another new hospital in the state in Kent County, and the Veterans Administration is now erecting a 400 bed hospital close to the center of Providence."

MR. JOHN E. FARRELL, Executive Secretary,
Rhode Island Medical Society,
106 Francis Street, Providence 3, R. I.

VERMONT—1946

VERMONT—1947



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Areas in Vermont Requesting General Practitioners

County	Town	Population
Franklin		29,401
Orange		17,048
Windsor		57,808

"While Vermont, with 398 active physicians to 359,231 population, has a ratio statewide of 1 physician to every 903 people, there is not an even uniformity of this ratio throughout the state, the more rural areas having a somewhat lower ratio of physicians to population. There has been relatively little migration of physicians in Vermont within the past year, but there has been an increase of active practitioners by 39, generally speaking graduates of the University of Vermont College of Medicine who had practiced a year or two in local communities before the war and who have returned to those places.

"We believe that probably the primary reason for our being able to maintain as satisfactory distribution of physicians as we have is the tendency for young men and women here in Vermont to attend the College of Medicine at the University of Vermont and return to their home communities to practice. The secondary reason would be the availability of hospital facilities in most areas. As a partial solution to the economic side of the problem of practice in rural areas, we are hopeful for results from the New Hampshire-Vermont Physician Service, sponsored by the Vermont State Medical Society, which is conducting enrolment campaigns on a community basis, which in our state means that the rural population will have an opportunity to participate."

Mr. John W. Brownlee, Executive Secretary,
Vermont State Medical Society,
128 Merchants Row, Rutland, Vt.

Official Notes

MUTUAL NETWORK BROADCASTS WILL NOT CLOSE

The summer season brings the cessation of broadcasts on the network of the National Broadcasting Company, but the Mutual Broadcasting System program will continue until November 17.

"Doctors—Then and Now," broadcast in cooperation with the National Broadcasting Company, was exceptionally well received by state medical societies, local radio stations and lay listeners and received a first award[1] in its class from the Institute for Education by Radio held at Ohio State University, Columbus, May 2-5. This program was based on regional broadcasts with participation of local medical societies and the origination of speakers at local radio stations in twenty-five areas of the continental United States. It dealt with medicine in the early years of the American Medical Association's hundred year history as compared with medicine today. Twenty-five physicians selected by state medical societies participated in the program.

The Mutual program "Stephen Graham—Family Doctor" is intended to portray to the lay listener some of the difficulties, problems, perplexities and heartbreaks of the physician, as well as his ethical and professional attitude toward patient, community, fellow practitioner and his profession. It is relatively light in educational medical features, since its purpose is to interpret the doctor rather than to educate the public in medical facts. This program too has received wide acceptance from radio stations, physicians and the public.

Extensive network broadcasting is costly. Although time is generously donated by the networks, the program costs must be assumed by the Association, and these are considerable. The Board of Trustees has authorized arrangements to be made for suitable sponsors who will join the Association in rendering public service through radio. This policy became effective in May, and thus far no programs have been sponsored commercially.

The American Medical Association wishes to express to the National Broadcasting Company and the Mutual network its appreciation for cooperation in the broadcasting of these two successful public service programs. To the Columbia Broadcasting System and the American Broadcasting Company, as well as National and Mutual, the Association extends its appreciation for liberal and friendly cooperation in broadcasting important features of the recent centennial meeting at Atlantic City.

1. Official List of Awards and Judges' Report for the Eleventh American Exhibition of Educational Radio Programs, May 2-7, 1947, sponsored by the Seventeenth Institute for Education by Radio, Ohio State University, Columbus 10.

Medical Legislation

STATE LEGISLATION

Alabama

Bill Passed.—S. 112, which passed the senate June 25, proposes the enactment of a law to regulate the handling, sale and distribution of barbiturates. The proposal would require prescriptions for barbiturates to be made only by a pharmacist on the original prescription of a person licensed to prescribe and administer barbiturates.

California

Bills Passed.—A. 1833, which passed the assembly June 12, to amend the labor code, proposes to define the word physician so as to include optometrists when relating to medical services rendered under the workmen's compensation act. A. 2352, which passed the assembly June 3, to amend the health and safety code, proposes to authorize a cemetery authority or a licensed funeral director to permit an autopsy of any remains in its custody on the receipt of a written authorization of a person representing himself to be the surviving spouse, a surviving child or parent, a surviving brother or sister, any other kin or person who has acquired the right to control the disposition of the remains, or the coroner or other duly authorized public officer. The proposal would also provide that the cemetery authority or licensed funeral director is not liable for permitting or assisting in making an autopsy pursuant to such authorization unless it has actual notice that the representation therein is untrue. S. 1239, which passed the house June 16, proposes the enactment of a chapter of the health and safety code for the purpose of licensing, inspecting and regulating public and private establishments which render to handicapped persons medical advice, diagnosis or treatment, physiotherapy, any form of muscle training, massage, etc.

Bills Enacted.—A. 2429, which has become chapter 867 of the Laws of 1947, to amend the business and professions code, authorizes licentiates of other states to act as resident or assistant resident physicians and surgeons in state hospitals for a period of not exceeding one year under certain circumstances. S. 809, which has become chapter 705 of the Laws of 1947, to amend the health and safety code, requires every licensed physician and surgeon or other person engaged in prenatal care of a pregnant woman, or attending such woman at the time of delivery, to obtain a blood specimen of such woman at the time of the first professional visit or within ten days thereafter and to submit such sample to an approved laboratory for a laboratory test for syphilis.

Nebraska

Bill Enacted.—L. B. 250, which was approved June 9, 1947, provides for the licensing, inspecting and regulating of hospitals and related institutions within the state and provides for the creation of a hospital licensing council.

New Hampshire

Bills Passed.—H. 370, which passed the senate June 18, proposes the enactment of a hospital survey and construction act requiring a survey of hospital facilities within the state and the preparation of a program for the construction of additional needed facilities. The proposal also requires the appointment of an advisory hospital council and authorizes the state board of health to apply for and accept federal funds for assisting the state in its hospital program. H. 371, which passed the senate June 18, proposes the enactment of a hospital licensing law. H. 449, which passed the senate June 12, proposes to require every physician attending a pregnant woman for conditions relating to the pregnancy to take or cause to be taken a sample of blood of such woman at the time of the first examination and to submit such sample to an approved laboratory for a standard serologic test for syphilis. H. 456, which passed the house June 23, proposes the creation of a mental hygiene commission to manage and conduct mental hygiene clinics primarily for the psychiatric and psychologic study and treatment of such children as may be committed to its care.

Wisconsin

Bill Introduced.—S. 19, to amend the law relating to the mentally ill and mentally deficient persons, epileptics, inebriates and drug addicts, proposes that the term "examining physician" as used in the act should mean one who is entitled to use the designation M.D.

Bill Passed.—S. 589, which passed the house June 12, proposes to authorize cooperative associations to establish and operate nonprofit plans for sickness care, including hospital care, for members through contracts with physicians, medical societies, hospitals and others.

Bills Enacted.—S. 185, which has become chapter 255 of the Laws of 1947, is a hospital survey and construction act requiring a survey of hospital and health facilities in the state and the preparation of a program for the construction of additional needed facilities. The law requires the appointment of an advisory hospital council and authorizes the state board of health to apply for and receive federal funds to assist in such survey and construction program. S. 156, which has become chapter 289 of the Laws of 1947, relating to the licensing of osteopaths, requires applicants for a license to practice osteopathy to have completed at least twelve months' internship in a reputable osteopathic hospital or its equivalent. S. 446, which has become chapter 399 of the Laws of 1947, requires all physicians and hospital authorities to report deaths, homicides, suicides, etc. to the sheriff, police officer or coroner of the county where such death takes place.

GOVERNMENT SERVICES

ARMY

ARMY TO BUILD RESEARCH CENTER

What is planned to be a great research center will be built for the Army Medical Department at Forest Glen, Md., near Washington, D. C., the War Department announced June 22. The initial cost is estimated at about $40,000,000. The Army District Engineer will supervise construction. The project will consist of a 1,000 bed general hospital, the Army Institute of Pathology, the Army Medical Museum and Center Administration building. Central Laboratory Group buildings and the Army Institute of Medicine and Surgery. A working library, quarters for the staff and an animal farm are included in the plans.

The new center will have close relationship to the Walter Reed Medical Center, the Naval Hospital, the medical schools of the District of Columbia and the proposed new District Medical Center, and it will cooperate with the Bureau of Standards, the National Institute of Health and the National Research Council.

Plans for the hospital building provide that 200 beds shall be specifically designated for research activities of the various institutes and central laboratories. However, they will remain an integral part of the hospital for service and patient care. The plans call also for a gymnasium, bowling alleys, swimming pool, auditorium, post exchange, post office, bank and game rooms, included in, or directly connected with, the hospital building.

The Institute of Pathology building will house the Department of Pathology, the American Registry of Pathology and the Army Medical Illustration Service. Extensive facilities for experimental research and teaching in pathology will be provided. The building will be connected with the Army Medical Museum and with the Central Laboratory Group. All research activities of the various groups will be correlated and the expanded Central Laboratory Group will serve research and teaching activities of all institutes.

The Administration Building will provide facilities for the administration of the entire center and will house the Army Medical Museum, the main auditorium, the research library and certain graduate teaching facilities.

The Central Laboratory Group will provide research and graduate teaching facilities for the entire center. These will be constructed as the need for them grows, the first being devoted to the service of the Institute of Pathology.

The Institute of Medicine and Surgery building will house the departments of Research Medicine, Research Dentistry, Veterinary Medicine, Research Surgery, X-Ray and Radiation and Preventive Medicine.

The center will bring together various medical units now scattered in various parts of the United States.

The architect-engineer contract for the proposed "Army Medical Research and Graduate Training Center" has been awarded jointly to New York and Washington firms as joint venturers.

NURSES NOMINATED FOR REGULAR ARMY COMMISSIONS

The President has sent to the Senate for confirmation the names of seventy-three nurses who have been nominated for permanent commissions in the Regular Army nurse corps. This is the first increment selected for commissions under the new law approved April 16. The nurses nominated have been serving on active duty in the Army, many of them for many years. The new appointment clarifies their status in the Regular Army. The ranks recommended for these nurses vary from the rank of Colonel to that of First Lieutenant, and included in the list is Col. Florence A. Blanchfield, who during the war was chief of the nursing division in the Surgeon General's Office and who is nominated for a permanent rank of Lieutenant Colonel.

ARMY AWARDS AND COMMENDATIONS

Brigadier General Elliott C. Cutler

The Oak Leaf Cluster to the Distinguished Service Medal has been awarded to Brig. Gen. Elliott C. Cutler, M. C., A. U. S., of Boston, for exceptionally meritorious service to his government in a duty of great responsibility from October 1942 to May 1945. The citation explains that, as chief surgical consultant, Headquarters European Theater of Operations, he was responsible for the development of adequate care of all wounded and injured in the theater, and to meet this great responsibility General Cutler developed and promulgated policies, instituted training programs, developed channels of free interchange of medical and surgical knowledge between medical officers of all Allied nations and by constant inspection of all echelons assured the highest standard of surgical care. General Cutler was a source of inspiration to the hundreds of surgeons at whose hands the American soldier received the finest care the world has ever seen. Dr. Cutler graduated from Harvard Medical School in 1913 and entered the service in World War II in July 1942.

Colonel Joseph F. Sadusk Jr.

The Typhus Commission Medal has been awarded to Col. Joseph F. Sadusk Jr., M. C., A. U. S., of New Haven, Conn. Colonel Sadusk rendered exceptionally meritorious service in connection with the United States of America Typhus Commission as executive officer of the special commission sent to the Southwest Pacific in September 1943, which commission conducted original investigations in New Guinea from October through December 1943. Colonel Sadusk had responsibility for most of the administrative matters of a scientific expedition working under campaign conditions in the Dobodura area at a time when scrub typhus was a disease of paramount military importance. He also made original and valuable contributions to the knowledge of the sources and mode of spread of scrub typhus, to the clinical characterization of the disease and to methods of treatment. His many sided contributions to the work of this commission assured its success and added new knowledge on the control and treatment of scrub typhus. Dr. Sadusk graduated from John Hopkins University School of Medicine in 1935 and entered military service in March 1942.

Colonel Hubert T. Marshall

The Legion of Merit has been awarded to Col. Hubert T. Marshall, M. C., A. U. S., who served in various capacities in the procurement of medical supplies and later as commanding officer, Army Medical Purchasing Office, from September 1943 to September 1945. He is recognized in the citation as having made a significant contribution to the successful accomplishment of the Medical Department's mission in World War II. During the period of Colonel Marshall's responsibility for procurement, many important items, such as penicillin and Japanese B encephalitis vaccine, were produced by industry for the first time. He played a significant role in the securing of an even flow of medical supplies without which the high standards obtained in the maintenance of the health of the Army and the care of casualties would not have been possible. He dealt with the many intricate problems of medical supply with courage, outstanding professional skill and a loyal devotion to duty. Dr. Marshall graduated from the University of Louisville School of Medicine in 1932 and entered the military service in December 1934.

Lieutenant Colonel Robert P. Rogers

The United States of America Typhus Commission Medal has been awarded to Lieut. Col. Robert P. Rogers, M. C., A. U. S., of Greenwich, Conn., whose citation mentions the meritorious service which he rendered in connection with the

work of the United States of America Typhus Commission during the epidemic at Naples and in southern Italy in the winter of 1943-1944. At that time he was on duty with the Allied Control Council. When his services were made available to the commission, he was placed in charge of the immunization section for the administration of typhus vaccine for the protection of individuals against infection. Through his efficient handling of this section, Lieutenant Colonel Rogers contributed to the success of the typhus control program in southern Italy. Dr. Rogers graduated from Harvard Medical School in 1925 and entered the military service in August 1942.

Major Richard P. Custer

The Army Commendation Ribbon has been awarded to Major Richard P. Custer, M. C., A. U. S., of Philadelphia. The citation read as follows: While on duty at the Army Institute of Pathology from Nov. 27, 1942 to Jan. 23, 1946 his outstanding professional skill and devotion to duty contributed in large measure to the professional success of the Army Institute of Pathology, especially as it is concerned with diseases of the blood-forming tissues and the lymphatic tumors. His studies and research have contributed to our knowledge of these diseases, which proved so important in the military service. Dr. Custer graduated from the Jefferson Medical College of Philadelphia in 1928 and entered the military service in November 1942.

Captain David Hochman

The Bronze Star Medal has been awarded to Capt. David Hochman, M. C., A. U. S., of Brooklyn, who as an assistant to the chief of professional services and surgery at the prisoner of war camps in Osaka, Japan, devoted untiring effort to improving the welfare of fellow captives from April 1944 to July 1945. The citation states that despite his own illnesses he performed services which did much to maintain the health and morale of his comrades. Dr. Hochman graduated from the School of Medicine, Royal Colleges of Edinburgh, Scotland, in 1939 and entered the military service in July 1941.

PUBLIC HEALTH SERVICE

THE ENLARGED CANCER CONTROL PROGRAM

With the passage of legislation bringing next year's budget of the National Cancer Institute, Bethesda, Md., to the all time high of $14,000,000, the U. S. Public Health Service announces plans for an expanded attack on the cancer problem.

Under authority of the Public Health Service law and the appropriation act, support may now be extended to universities to assist in developing greatly expanded cancer research and training programs. The law also supports the acquisition of land and construction of buildings when urgently needed. Under a provision of the act, funds for cancer research and training grants remain available until spent.

Four million dollars of the increase in the budget will go to cancer control, the program administered through the states to increase the effective use of present methods of diagnosing and treating cancer. The cancer control program will place emphasis on the improvement of cancer detection, diagnostic and treatment facilities, the development of refresher courses for doctors, the establishment of adequate statistical services on cancer and the setting up of a cancer control units in state health departments.

In connection with the expanded program Dr. Harry Eagle has been appointed director in charge of research within the institute and Dr. David E. Price in charge of cancer research grants. Dr. Austin V. Deibert also joins the program in charge of cancer control. Dr. Eagle comes to the institute from Baltimore, where he was director of the Laboratory of Experimental Therapeutics, a joint project of the U. S. Public Health Service and the Johns Hopkins School of Hygiene. He has made important research contributions in immunity and serologic tests for syphilis. Dr. Price was formerly in the Research Grants Division of the National Institute of Health, and Dr. Deibert was in charge of cancer control before its recent transfer to the Cancer Institute from the Bureau of States Services of the U. S. Public Health Service.

OFFICERS RELEASED FROM SERVICE

U. S. Public Health Service headquarters reports that the following medical officers have been terminated, inactivated or retired and directed to proceed to the city opposite their names:

Boyd, Dewitte T., S. A. Surgeon (R), Hermiston, Ore.
Card, William J., S. A. Surgeon (R), Chattanooga, Tenn.
Holloman, Alfred L., Surgeon, Frederick, Okla.
Jenkins, Edward C., Surgeon, Pinehurst, N. C.
Koplin, Allen N., S. A. Surgeon (R), New York.
Reiter, Adolph F., Surgeon (R), McKeesport, Pa.
Stanulonis, Stanley W., Surgeon (R), Shenandoah, Pa.

CLOSE MARINE HOSPITAL

According to an announcement by the Surgeon General May 20, the U. S. Public Health Service decided to close the 90 year old Marine Hospital at Evansville, Ind., June 30. The decision was based on the findings of a special board that the hospital had operated at only 50 per cent capacity for the last two years, that patient costs are excessive and that the two wings are fire hazards.

MISCELLANEOUS

VOCATIONAL REHABILITATION PROGRAM

More than 160,000 disabled civilians have been prepared for and placed in paying jobs since the civilian vocational rehabilitation program was expanded four years ago, director Michael J. Shortley announced on the fourth anniversary of the legislation which led to the establishment of the Office of Vocation Rehabilitation. The vocational rehabilitation program through which these civilians became wage earners and tax payers was maintained at an average cost of about $300 per rehabilitated case. The total annual earnings of the disabled men and women who were rehabilitated in the 1946 fiscal year were estimated at about $11,600,000 when they contacted the state agencies; after rehabilitation the rate of annual earnings of these workers —excluding family workers and farmers—was an estimated $56,300,000, or an increase of almost 400 per cent. Public Law 113 amended the original law so that mentally handicapped civilians became eligible for state-federal vocational rehabilitation services, as well as the physically disabled. It also provided authority for the use of medical, surgical and psychiatric treatment to reduce or remove job handicaps resulting from physical or mental disability—a provision which was lacking in the original law.

SALE OF SURPLUS GOVERNMENT PROPERTY

About $1,500,000 worth of pentothal sodium is being offered for sale by the War Assets Administration at new low fixed prices up to July 28. The pentothal sodium is in 0.5 and 1 gram ampules, packed in boxes of twenty-five ampules of the anesthetic and twenty-five ampules of sterile distilled water. Each case contains twelve boxes, and the price f. o. b. is $50 per case for the 0.5 Gm. ampules and $80 for 1 Gm. ampules.

Regional Office, 404 South Wabash Avenue, Chicago 5. Sale of hypodermic needles. Sale opens July 21 and is continuous.

PHYSICIANS SEPARATED FROM SERVICE

ARMY MEDICAL CORPS OFFICERS RECOMMENDED FOR/OR RELIEVED FROM ACTIVE DUTY

Alabama

Dumas, James F.....Foley
Gay, Otis F.....Greenville

Arizona

Johnston, Charles L. Jr.....San Luis

Arkansas

Clark, James F.....No. Little Rock
Gordy, Luther F. Jr.....Conway
Mayfield, George C.....Hot Springs
Toombs, Vernon L.....Gurdon

California

Crall, Herbert D.....San Francisco
Davis, David S.....Los Angeles
Davis, Irving.....San Francisco
Dawson, George L.....Napa
Fisher, Harold L.....Santa Cruz
Gladen, Ralph G.....Patton
Hutner, Laurence M.....Beverly Hills
Kieffner, Richard G.....Los Angeles
Koerper, Carl W.....Oakland
Mikita, Michael M.....Oakland
Nowack, Jacques.....San Francisco
Ostich, Nathan H.....Los Angeles
Paisley, Charles B.....Inglewood
Rabinowitz, David L.....Los Angeles
Rickard, Vernon.....Los Angeles
Roberts, Nathaniel E.....Los Angeles
Walters, Harold E.....San Jose
Wololan, Jeremiah J.....Berkeley

Colorado

Keefe, John A.....Denver
Roadruck, Roscoe D.....Salida
Shea, John D.....Denver

Connecticut

Griswold, Dwight.....Old Lyme
Ingenito, Gabriel A.....New Haven

District of Columbia

Brandes, Herbert G.....Washington
DeSausseure, Richard L. Jr...Washington
Gray, Augustus C.....Washington
Rogers, John S.....Washington

Florida

Elmendorf, John E. Jr.....Jacksonville
Waldred, Jack M.....Leesburg

Georgia

Coward, Allen W.....Augusta
Hummel, John E.....Augusta
Mashburn, Marcus Jr.....Cumming
Rabun, John B.....Augusta
Ward, William C.....Atlanta

Idaho

Rigby, Elmer C.....Idaho Falls

Illinois

Barnes, Kenneth O.....Chicago
Crandle, Ellis R.....Carbondale
Davis, Dave.....Chicago
Eisele, Paul L.....Naperville
Faingold, Joseph E.....Chicago
Grams, Leslie R.....Chicago
Harroun, John E.....Chicago
Kocour, Elmer J.....Chicago
Massover, Alfred J.....Chicago
Metro, Michael L.....Alton
Michet, Clement J. J.....Chicago
Sarver, Francis E.....Chicago
Schroeder, Paul L.....Oak Park
Seaman, William B.....Chicago
Siler, George B.....Oak Park
Voltz, Vernon C.....Rockwood
Watson, James.....Chicago
Weigel, William J.....River Forest

Indiana

Beeler, John W.....Indianapolis
Bloomer, Richard S.....Rockville
Eades, Ralph C.....Valparaiso
Ference, Edward G.....Whiting
Graves, John W.....Indianapolis
Klaus, Julius M.....Gary
Marshall, William P.....Indianapolis
Nowak, Henry J.....Indianapolis
Owsley, Guy A.....Hartford City
Schlaegel, Theodore F. Jr...Indianapolis
Schmidt, Robert L.....Evansville
Seal, Perry F.....Indianapolis
Sheridan, Joseph L.....Kokomo
Steele, Paul W.....Indianapolis
Toth, John J.....Whiting

Iowa

Berryhill, Melvin B.....Buffalo Center
Bruner, Julian M.....Des Moines
Glesne, Orvin G.....Knoxville
Kersten, Herbert H.....Fort Dodge
Klenzle, William K.....Gladbrook
Midkiff, Carl M.....Iowa City
Stamler, Frederic W.....Muscatine
Walvoord, Carl A.....Dunlap
Waterman, Franklin M.....Ruthven
Wolfe, Otis D.....Marshalltown

Kansas

Anderson, Arthur S.....Lawrence
Blackburn, Lewis C.....Eudora
Gibbons, Edward H.....Topeka

Kentucky

Myers, Ernest E.....Lexington
Rutledge, Charles C.....Richmond
Weeter, John C.....Louisville

Louisiana

Foley, Thomas H.....Plaquemines
Haik, George M.....New Orleans
Lafleur, Nathan C.....Opelousas
McBride, Wallace M.....Crowley
Yeager, John M.....Alexandria

Maryland

Dausch, Michael J.....Paltimore
Mohr, Walter C.....Baltimore
Robbins, Martin A.....Baltimore
Roseman, Ephraim.....Baltimore

Massachusetts

Clancy, Arthur W.....Newbury Port
Harris, Albert E.....Northampton
Michell, León G. II.....Lynn
Nereo, Oswaldo A.....Quincy
O'Brien, Dalton C.....Cambridge
Valliere, Joseph L.....Chatham

Michigan

Antell, Gunnard J.....Negaunee
Bartlett, Walter M.....Benton Harbor
Davis, David B.....Grand Rapids
Grant, Joseph O.....Detroit
Keyes, James T.....Saginaw
Kleber, John A.....Detroit
Lepisto, Victor E.....Wakefield
Pott, Abraham.....Grand Rapids
Roney, Eugene H.....Detroit
Thompson, Arthur B.....Saginaw

Minnesota

Michel, Henry H.....Minneapolis
Murray, Robert A.....Parkers Prairie
Picha, Richard H.....Hopkins
Pratt, Fred J. Jr.....Minneapolis

Mississippi

Butler, George H.....Liberty
Ellis, Donald R.....Columbus
Hall, James L.....Vicksburg
Hughes, James A.....Gulfport
Rotenberry, Clinton G.....Oxford
Shettles, Landrum B.....Pontotoc

Missouri

Banner, Richard E.....Kansas City
Lischer, Carl E.....Webster Groves
Riggs, George T.....Amity

Nevada

Hartman, Charles F.....Reno

New Mexico

Shortle, James S.....Albuquerque

Ohio

Boggs, Joseph D.....Bellefontaine
Bond, Robert G.....Springfield
Curtiss, Edgar J.....Lima
Dingle, John H.....Cleveland
Lawless, Edward C.....Columbus
Meredith, Roy M.....Marietta
Michals, Arnold A.....Cleveland
Muenzer, Robert W.....Elmore
Rock, Harry A.....Chillicothe
Schoenling, John E.....Cincinnati
Steinberg, Abraham H.....Toledo
Williams, Edward T.....Norwalk

Oklahoma

Archer, Homer V.....Oklahoma City
Payne, Richard W.....Oklahoma City
Walker, Dean C.....Pawhuska

Oregon

Ball, Wendell L.....Portland
Carter, Paul I.....Portland
Leong, Richard W.....Portland
McKelvey, Gilbert J.....Portland
Olsen, Ralph L.....Portland
Taylor, Douglas H.....Cloverdale

Rhode Island

Kaiser, Alfred J.....Warren

South Carolina

Creech, Clarence M.....Spartanburg
Lucas, Thomas L.....Chesterfield
Rourk, Malcolm H.....Myrtle Beach

South Dakota

Welty, Dalton M.....Hot Springs

Tennessee

Little, Joseph A.....Nashville
Tacket, Hall S.....Memphis
Westphal, Kean F.....Memphis

Virginia

Davis, Algernon C.....Roanoke
Martin, Berkeley H. Jr.....Richmond
Meyer, George I.....Roanoke
Shaver, Jack S.....Maurertown
Volkin, Leonard B.....Petersburg
Wilson, Robert M. Jr.....Richmond

Alaska

Charteris, William C.....Sitka

Puerto Rico

Gonzalez, Louis.....Santurce
Melendez, Pedro C.....Bayamon
Navarro, Felix A.....Bayamon
Sugranes, Jose G.....Maunabo

Liberia

Ricketts, Edwin T.....Harbel

Medical News

(Physicians will confer a favor by sending for this department items of news of general interest: such as relate to society activities, new hospitals, education and public health. Programs should be received at least two weeks before the date of meeting.)

CALIFORNIA

University to Expand Medical Center.—The University of California, Berkeley-San Francisco, has purchased 90 acres of land for the contemplated $30,000,000 expansion of its San Francisco Medical Center on Parnassus Heights. Half of the funds needed for the projected expansion have been provided by the state legislature, and plans are nearing completion for a new medical sciences and hospital building.

Tuberculosis Survey in Chinatown.—The San Francisco Tuberculosis and Health Association and San Francisco and state departments of public health are carrying out a tuberculosis case finding program in San Francisco's Chinatown area. X-ray equipment from the state department of public health has been set up in the Chinese Hospital and test plates are being taken five days each week. Local physicians are referring patients to the x-ray center, and the epidemiology is being done by public health nurses of the San Francisco Health Department. Chinatown had a tuberculosis mortality rate last year of 138.9 deaths per hundred thousand of population compared to the entire state rate of 48 for the same period.

CONNECTICUT

New Dean of College of Pharmacy.—Harold G. Hewitt, Ph.D., for twenty-one years with the department of chemistry, University of Buffalo, has been appointed dean of the College of Pharmacy at the University of Connecticut, effective July 1. He is president of the Section on Chemistry, American Association of Colleges of Pharmacy.

Society News.—Dr. Creighton Barker, New Haven, executive secretary of the Connecticut State Medical Society and secretary to the Connecticut Medical Examining Board, has been elected president of the Connecticut Cancer Society. Ira V. Hiscock, Sc.D., chairman of the department of public health at Yale University, was elected vice president, and Miss Grace Mooney, executive assistant of the state medical society, secretary.

DISTRICT OF COLUMBIA

University Appointments.—On July 1 Dr. Edward B. Tuohy, Rochester, Minn., became director of the department of anesthesiology at Georgetown University School of Medicine. He is a graduate of the University of Pennsylvania School of Medicine, Philadelphia, 1932, and has been a member of the staff of the Mayo Foundation for many years. He succeeds Dr. Fred R. Sanderson, resigned, who will retire but continue on the staff of the university as clinical professor of surgery. Dr. Robert J. Coffey became professor of surgery July 1. A graduate of Georgetown University School of Medicine, 1932, he has recently been professor of experimental surgery and instructor in clinical surgery at Georgetown.

FLORIDA

Donner Hall at Palm Beach.—The Donner Foundation, Inc., has deeded a $150,000, sixty-four room building in Palm Beach, Fla., to the Institutum Divi Thomae, Cincinnati, for scientific research. The building, to be known as Donner Hall, was formerly a part of the estate of the late Col. E. R. Bradley and is adjacent to the Institutum's Marine Biological Laboratories. Donner Hall will provide quarters for a marine biophysics laboratory for intensive fundamental research in cancer and quarters for visiting scientists from various parts of the world, who will be invited to participate in a series of symposiums devoted to different fields of research. The Institutum Divi Thomae, founded in 1935 by the archbishop of Cincinnati, is a graduate research school with fourteen affiliated units throughout the United States. William H. Donner, 83, a millionaire Philadelphia steel man who has previously given large sums to cancer study, is director of the Donner Foundation.

IDAHO

State Medical Election.—At the annual meeting of the Idaho State Medical Association at Sun Valley, June 19, Drs. Albert B. Pappenhagen, Orofino, became president, Franklin B. Jeppesen, Boise, president-elect and Wallace Bond, Twin Falls, secretary-treasurer. The 1948 annual meeting will be held at Sun Valley.

ILLINOIS

Emergency Water Supply Insured in Case of Disaster.—The first of six water purifiers capable of meeting the emergency needs in case of disaster in Illinois communities has been received by the state department of health from the American Red Cross. The gas engine driven purifiers are capable of purifying 15 gallons of water per minute and are a part of the disaster preparedness operations in Illinois. Purchased from the War Assets Administration by the Red Cross, the purifiers will be located at strategic points throughout the state. The purifiers are familiar to thousands of American soldiers who served overseas in areas where water from ponds and polluted streams had to be purified for drinking and cooking purposes.

Chicago

Illinois Professors to Retire.—The following retirements at the University of Illinois College of Medicine, Chicago, have been announced, effective September 1: William H. Welker, Ph.D., head of the department of biologic chemistry, who has been on the faculty since 1913 and chairman of the committee on graduate study; Dr. Dietrich Klemptner, an associate in medicine, who joined the university faculty in 1928; Dr. Charles Phifer, professor of surgery, who has taught at Illinois since 1913; Dr. Herman L. Kretschmer, professor of urology, and Dr. Kellogg Speed, professor of surgery, who joined the staff in 1941, when Rush Medical College affiliated with the University of Illinois.

Dr. Luckhardt Made a Distinguished Service Professor.—Dr. Arno B. Luckhardt, professor of physiology at the University of Chicago School of Medicine and discoverer of ethylene gas as an anesthetic, has been designated distinguished service professor of physiology at the university. Dr. Luckhardt received his Ph.D. from the University of Chicago, 1911, his M.D. from Rush Medical College, and honorary degrees from Conception College, Conception, Mo., and Northwestern University, Evanston. He was appointed instructor in physiology in 1912, was made a professor in 1923, and has received the Callahan memorial award for accomplishments in medical research. He is a past president of the American Physiological Society and of the Federation of American Societies for Experimental Biology.

MASSACHUSETTS

Public Health Appointments.—The following appointments have been announced by the state department of health, Boston: as epidemiologists, Drs. Victoria M. Cass; Claire F. Ryder, Brooks Ryder and Joseph H. Hanson. Dr. Nicholas J. Fiumara has been promoted to director, division of venereal diseases, pending qualification by civil service.

Helen Putnam Fellowship Award.—Dr. Frances J. Bonner, Boston, was awarded the Helen Putnam Fellowship for advanced research in genetics or in mental health for the second and final year at commencement exercises, Radcliffe College, June 4. Dr. Bonner was the first recipient of this fellowship, which carries a stipend of $2,000 and is open annually to a mature woman scholar qualified to carry on significant research or creative work. She graduated at Boston University School of Medicine, 1943, and is a research fellow in neuropathology at Harvard Medical School. She will continue research which she has been carrying on during the present academic year on the hereditary factors in hysteria.

MISSOURI

Jackson County Installation Banquet.—More than 350 members of the Jackson County Medical Society attended the sixty-fifth annual installation banquet in Kansas City June 26. Dr. Robert L. Hoffman was installed as president. Rev. Thomas McCartan Knapp, S. J., president of Rockhurst College, Kansas City, spoke on "The Soul and the Doctor." Recognition of the centennial year of the American Medical Association was made by the inclusion inside the program cover of four of the special three cent stamps bearing the reproduction of the painting "The Doctor." Two laymen were presented gold keys and citations. Mr. Arthur B. Eisenhower, vice president of the Commerce Trust Company, was cited for his leadership in the Jackson County cancer fund campaign, and Conwell Carlson, reporter for the Kansas City *Star*, was cited for "lifting the curtain on medical news in Kansas City." The society has a membership of 680.

NEBRASKA

State Medical Election.—At the May annual meeting of the Nebraska State Medical Association Dr. George E. Charlton, Norfolk, became president, and Dr. James E. M. Thomson, Lincoln, was made president-elect; Drs. Milton H. Carrig, Bloomfield, and Earle E. Farnsworth, Grand Island, vice presidents; Roy B. Adams, Lincoln, secretary, and Mr. M. C. Smith, Lincoln, executive secretary.

Appoint Head of New County Health Department.—Dr. Corinne S. Eddy is health director for the newly created Lincoln and Lancaster County Health Department. The new unit is an extension of the Lincoln City Health Department, authorized by the legislature to include all Lancaster county citizens. Dr. Eddy received her Ph.D. at the University of Chicago and her medical degree from the University of Illinois College of Medicine, Chicago. She has done public health work in Alabama and Mississippi.

NEW MEXICO

State Medical Election.—At the annual session of the New Mexico Medical Society in May Dr. Victor K. Adams, Raton, became president. Philip L. Travers, Santa Fe, was named president-elect, and H. L. Jamary, Albuquerque, secretary-treasurer.

NEW YORK

Meeting of School Physicians.—New York State's Association of School Physicians and the School Nurse Teachers Association will meet with the Annual Conference of Health Officers and Public Health Nurses at the Grand Union Hotel, Albany, July 28. The presidential address will be given by Dr. Edgar Bieber, Dunkirk. Dr. Francis H. Marx, Oneonta, will speak on "The Wetzel Grid"; Dr. Konrad E. Birkhaug, New York State Department of Health, Albany, on "BCG Vaccination"; Col. Herbert Pollack, New York, "Malnutrition in the Armed Forces and in Concentration Camps and Its Significance in the School Health Program," and Dr. Albert D. Kaiser, health officer, Rochester, "The Spastic Child and the School."

Tristate Medical Meeting.—Chautauqua County Medical Society will sponsor its twelfth annual interstate medical meeting at the Chautauqua Institution grounds at Chautauqua Lake July 24. On the medical program Dr. Abraham H. Aaron, moderator, William F. Lipp and Leon J. Leahy, all of Buffalo, and George W. Crile, Cleveland, will participate in a discussion of peptic ulcer. The "Present Status of Thyroid Disease" will be discussed by Dr. Crile and Dr. John H. Talbott, professor of medicine at the University of Buffalo Medical School; and Dr. Paul D. White, Boston, will speak on "Recent Advances in Our Knowledge of Heart Disease." Physicians from western New York, northwestern Pennsylvania and the northeastern corner of Ohio are invited to attend.

New York City

Personal.—Dr. Adolph G. Kammer, Oak Ridge, Tenn., has been appointed director in charge of the medical activities of all plants of Carbide and Carbon Chemicals Corporation and will be located at South Charleston, W. Va. He is a graduate of the University of Pennsylvania School of Medicine, 1928. ——Dr. Burton L. Zohman has been appointed attending physician to the Long Island College Division of Kings County Hospital in Brooklyn and associate professor of clinical medicine at the Long Island College of Medicine.——Dr. Harold A. Abramson, assistant professor of physiology, Columbia University College of Physicians and Surgeons, and associate physician for allergy, Mount Sinai Hospital, has been appointed consulting physician for allergy at the Sea View Hospital, Staten Island.

Dr. Loeb Made Bard Professor of Medicine.—Dr. Robert F. Loeb has been appointed Bard professor of medicine at Columbia University College of Physicians and Surgeons and director of the medical service at Presbyterian Hospital effective July 1, succeeding Dr. Walter W. Palmer, who became emeritus professor and a consultant of the Presbyterian Hospital. Dr. Loeb received his medical degree from Harvard Medical School, Boston, 1919. He has been associated with Presbyterian Hospital for many years and was associate medical director of the Neurological Institute 1938-1941. In 1942 he became Lambert professor of medicine and attending physician at Presbyterian Hospital. During the late war he was a consultant to the Office of Scientific Research and Development and chairman of the Board for the Coordination of Malarial Studies, charged with the responsibility of developing new drugs for the management of malaria. He recently served as chairman of the Board of Review of the United States Atomic Energy Commission. He is chairman of the Fellowship Board of the National Research Council and a past president of the American Society for Clinical Investigation.

OHIO

License Revoked.—Dr. Lloyd L. Jones, Columbus, has been convicted of criminal abortion by the Franklin County Court of Common Pleas, and his certificate to practice medicine was revoked by the board, according to the *Ohio State Medical Journal*.

Personal.—Dr. Thomas A. Gardner, Springfield, assistant public health director of the city since last October, assumed his duties recently as director of health.——Dr. Drew L. Davies, Columbus, has been appointed national chairman of the services on first air, water safety and accident prevention of the American Red Cross.

Hospital News.—Contracts have been recently let for the construction of a 105 bed hospital addition at the Stillwater Sanatorium (District Tuberculosis Hospital) at Dayton, jointly operated by Montgomery and Preble counties. The superintendent of the 107 bed hospital is Dr. Everett F. Conlogue.

UTAH

Appoint Head of Department of Obstetrics and Gynecology.—Dr. Emil G. Holstrom, associate professor in the department of obstetrics and gynecology, has been named professor and head of the department to succeed Dr. Charles E. McLennan, who has accepted an appointment as chairman of the department of obstetrics and gynecology at Stanford University School of Medicine, Stanford University-San Francisco. A graduate of the University of Minnesota Medical School, Minneapolis, 1938, he was a teaching fellow in obstetrics and gynecology at Minnesota University hospitals. He was on the staff of Salt Lake General Hospital, and later an instructor in his field at the University of Minnesota School of Medicine, Minneapolis, 1942-1943, and from there came to the University of Utah School of Medicine as an associate professor.

Cancer Research.—A total of $25,805 has been allocated to the University of Utah School of Medicine, Salt Lake City, by the American Cancer Society in the form of three research grants and one fellowship. This includes $3,000 per annum to be given to Dr. Charles M. Huguley Jr., fellow in medicine under the guidance of Dr. Maxwell M. Wintrobe, professor and head of the department of medicine; $4,560 allotted to Dr. Wintrobe for the study of halogenated amines and related compounds and of irradiation in the management of leukemia, Hodgkin's disease and lymph node diseases, and $10,395 granted to Dr. George Sayers, Ph.D., for work on urinary output and adrenocorticotropin and regulation of pituitary adrenocorticotropic activity. The remainder was granted to support a study by Dr. H. Henry Lerner, professor and head of the department of radiology, on the protective and therapeutic action of roentgen radiation and chemical agents in mice with experimental leukemia and lymphosarcoma.

WISCONSIN

University to Repeat Infantile Paralysis Course.—The University of Wisconsin Medical School, Madison, will repeat the intensive course in the diagnosis and therapy of poliomyelitis July 21-26 at the Medical School and the State of Wisconsin General Hospital as well as the Wisconsin Orthopedic Hospital for Children. Again this course is being presented by the medical school in cooperation with the county chapters of the National Foundation for Infantile Paralysis, Inc., throughout Wisconsin. Thirty-three physicians attended the course during its first offering. Details can be obtained from Dr. Llewellyn R. Cole, Coordinator of Graduate Medical Education, Medical School, University of Wisconsin, 418 North Randall Avenue, Madison 6, Wis.

WYOMING

State Medical Election.—At the meeting of the Wyoming State Medical Society in Sheridan June 23-25 Dr. Emory W. DeKay, Laramie, became president. Dr. George E. Baker, Casper, was named president-elect; Drs. Dewitt Dominick, Cody, vice president; George H. Phelps, Cheyenne, secretary, and Peter M. Schunk, Sheridan, treasurer. Mr. Arthur Abbey of Cheyenne was appointed executive secretary, and Dr. E. Earl Whedon, Sheridan, is the newly appointed editor of the state journal.

PUERTO RICO

Committee Studies Need for Doctors and Nurses.—A joint committee of the Puerto Rico Medical Association and lawmakers is undertaking a comprehensive survey of the needs of doctors and nurses here. All the government agencies and municipalities have been contacted in an effort to recommend measures against the shortage in these professions and to improve medical services. The committee is composed of Drs. Juan A. Pons, health commissioner; A. Oliveras Guerra, Manuel Astol, Jerenfel Cordero, representing the Puerto Rico Medical Association and the department of health, and Senators Vicente Geigel Polanco, Francisco Anselmi and Adolfo Monserrate. A list of all vacancies for doctors in government institutions and municipalities is being prepared as well as a list of all young medical students now studying medicine in continental United States and other countries. The list comprises also all medical students who have graduated through scholarships offered by the University of Puerto Rico and other institutions here as well as data on foreign physicians who are now working for government institutions in the island.

GENERAL

Board of Pathology Examination.—The American Board of Pathology has declared that after Jan. 1, 1948 all applicants for certification will be required to take the examinations of the board. The last meeting of the American Board of Pathology before this date will be October 24-25 in Chicago.

New Society for Study of Arteriosclerosis.—The American Society for the Study of Arteriosclerosis was created in Atlantic City, June 9. Dr. Wilhelm C. Hueper, New York, was elected president, William B. Kountz, St. Louis, vice president, and Dr. Otakar J. Pollak, Wilmington, Del., secretary-treasurer.

Opium Traffic Increases.—Traffic in prepared opium has been rising since 1944, the federal narcotics commissioner, Washington, D. C., said June 7 in his report for 1946. The aggregate weight of seizures at the borders and ports was 22,471 ounces, compared with 9,567 in 1945. Most of the raw opium seized, it was said, originated in Iran.

National Medical Association Meeting.—The fifty-second annual convention of this association will meet at the Jefferson High School, Los Angeles, August 18-22 under the presidency of Dr. Walter A. Younge, St. Louis, as guests of the Southern California Medical, Dental and Pharmaceutical Association. There will be general meetings, section meetings, round table discussions and a program of entertainment. The annual oration in medicine will be given by Dr. William G. Tyson, Savannah, Ga., on "Cryptorchism and Gynecomastia."

New Foundation for Research in Rheumatic Fever.—An announcement was made July 7 of the formation of the Helen Hay Whitney Foundation for basic scientific research in rheumatic fever. The distributing committee of the foundation are Mrs. Charles S. Payson (Joan Whitney), New York; John Hay Whitney, New York; Frederick K. Trask Jr. and William Harding Jackson, New York. Dr. T. Duckett Jones, Boston has been appointed medical director of the foundation with temporary offices in the New York Hospital, 525 East 68th Street, New York. Dr. Jones stated that the purpose of the foundation is to make possible research which may increase our knowledge of rheumatic fever.

Cancer Foundation Names President.—Abbott Kimball, president of Abbott Kimball Company, Inc., New York, on June 3 accepted the presidency of the National Cancer Foundation, Inc., created last May "to press for government action against cancer and to lead other activities seeking care of cancer victims not now handled by an organized group." Mr. Kimball has served as treasurer of the foundation. He succeeds Julius J. Perlmutter. The foundation expects to establish a series of advanced cancer hospitals throughout the United States. The foundation, with headquarters at 85 Franklin Street, New York, has just been granted a charter as a corporation under the laws of the state of New York.

Dr. Eliot on Leave from Children's Bureau.—The United Nations is to conduct a survey of the relief programs being carried out in seven central and eastern European countries by its International Children's Emergency Fund, under the direction of Dr. Ludwig Rajchman, chairman of the board, which operates the emergency fund. Dr. Martha M. Eliot, associate chief, U. S. Children's Bureau, and president-elect of the American Public Health Association, now on leave from the bureau, will be chief medical consultant. A group of four health and medical officers will spend several weeks touring children's institutes and inspecting other facilities. It is expected that the Emergency Fund will help feed 20,000,000 children through the national relief services which have been set up in each country.

Nutrition Awards.—The American Institute of Nutrition made two awards at its annual dinner in Chicago May 19. The Borden award for 1947 was presented to Leonard A. Maynard, Ph.D., Ithaca, N. Y., for contributions to the physiology of milk secretion, factors affecting milk production and milk composition, and the requirements of animals for dietary fats. The Mead Johnson and Company award for research on the vitamin B complex was presented to Dr. William J. Darby, associate professor of biochemistry, Vanderbilt University School of Medicine, Nashville, Tenn., Paul L. Day, Ph.D., professor of physiologic chemistry, University of Arkansas School of Medicine, Little Rock, and E. L. Robert Stokstad, Ph.D., research chemist, Lederle Laboratories, Pearl River, N. Y., for their investigations on B complex vitamins with special reference to studies on the chemistry and nutritional significance of folic acid.

Prevalence of Poliomyelitis.—Reports of cases of poliomyelitis for the periods indicated have been received from the division of public health methods, U. S. Public Health Service:

Division and State	Week Ended			Total to		Total *	
	July 5, 1947	July 6, 1946	Median, 1942-1946	July 5, 1947	July 6, 1946	March 15, 1947	March 16, 1946
New England:							
Maine	1	1	0	7	3	4	3
New Hampshire	0	1	0	5	3	1	2
Vermont	0	0	0	8	7	0	3
Massachusetts	2	0	0	12	7	5	3
Rhode Island	2	0	0	6	0	5	0
Connecticut	0	2	2	8	15	5	7
Middle Atlantic:							
New York	8	10	10	89	113	53	80
New Jersey	4	2	2	20	21	14	15
Pennsylvania	1	2	1	19	32	5	30
East North Central:							
Ohio	6	8	5	28	47	18	32
Indiana	1	2	2	21	18	5	13
Illinois	3	13	5	49	79	27	71
Michigan	3	1	1	38	16	14	6
Wisconsin	0	0	0	24	16	0	3
West North Central:							
Minnesota	2	20	2	25	41	12	40
Iowa	0	7	2	18	23	10	24
Missouri	1	13	1	24	35	14	28
North Dakota	0	0	1	18	3	13	3
South Dakota	0	0	0	2	3	0	3
Nebraska	3	3	0	30	7	23	6
Kansas	1	4	2	21	37	3	33
South Atlantic:							
Delaware	0	0	0	1	1	1	1
Maryland	0	1	0	12	1	6	3
District of Columbia	0	0	0	3	1	1	0
Virginia	3	1	1	19	10	9	4
West Virginia	0	0	0	5	8	1	5
North Carolina	1	5	1	22	37	7	30
South Carolina	1	0	0	4	11	3	8
Georgia	2	15	4	18	46	11	28
Florida	0	32	2	48	314	23	265
East South Central:							
Kentucky	0	4	2	13	24	12	21
Tennessee	0	4	4	18	22	6	13
Alabama	0	25	5	27	122	10	119
Mississippi	0	7	1	22	45	5	28
West South Central:							
Arkansas	0	11	3	20	38	10	26
Louisiana	4	14	3	33	86	15	67
Oklahoma	0	10	6	20	49	9	43
Texas	3	45	21	72	337	47	309
Mountain:							
Montana	2	1	0	4	24	2	8
Idaho	0	0	0	13	3	3	1
Wyoming	0	1	0	4	2	1	1
Colorado	1	22	1	16	104	11	103
New Mexico	1	1	0	6	16	3	15
Arizona	0	3	0	11	10	8	7
Utah	0	1	0	1	13	0	7
Nevada	0	0	0	0	0	0	0
Pacific:							
Washington	2	2	0	25	58	17	25
Oregon	0	0	0	9	5	4	1
California	31	17	17	377	236	228	149
Total	93	311	..	1,395	2,163 †	684	1,696
Median, 1942-1946	..	...	345	1,329		•	

* Last two columns show incidence since approximate seasonal low week (week ended between March 15 and 21).
† Figures changed by corrected reports.

Medical Women's Library Fund.—The American Medical Women's Association is planning to raise $500,000 to erect a building for the Medical Women's Library, which came into its possession in 1933. The Woman's Medical College of Pennsylvania, Philadelphia, donated the site and will assume responsibility for its upkeep. The collection was presented to the American Medical Women's Association by Dr. Bertha Van Hoosen, Chicago, at the close of the Century of Progress exposition and has been housed in the Quine Library, 1853 Polk Street, Chicago. A trained librarian gives half time service to the supervision and upkeep of files, correspondence, books, manuscripts, press notices and other details. The library collects articles or information by or about women in science and maintains up to date information concerning women physicians and material memorializing pioneer women of science. It functions through a committee. Annual or life memberships may be secured for $10 and $100, respectively, book memberships for $2 or Sadler Memorial Memberships for $1. Checks may be made to Dr. Bertha Van Hoosen, Chairman, American Medical Women's Association, 25 East Washington Street, Chicago.

Foreign Group to Study American Blood Program.—Scholarships for the study of blood and its derivatives have been offered to a selected group from foreign countries by the American Red Cross in cooperation with the League of Red Cross Societies. The candidates will be proposed by the national Red Cross societies and will be selected on a basis of personal and professional qualifications as well as on the need in their country for information on the use of blood fractions. The scholarships will be for nine to twelve months of study in the United States and will have a value of $2,500-$3,000. The training will include study of method of recruiting donors, collecting and processing blood, processing plasma and the uses of blood and blood derivatives in medicine and public health. Field work will be done in North Dakota for mobile field laboratory operation, in Michigan for its state plan of plasma fractionation and in Miami, Fla., for private blood bank maintenance. Details of the training were worked out by Dr. Warren F. Draper, Washington, D. C., assistant administrator, Medical Services, American Red Cross, in cooperation with Dr. Charles A. Janeway of Boston, chairman of the Red Cross Advisory Committee on Blood and Blood Derivatives.

Appoint Epidemic Coordinator.—The National Foundation for Infantile Paralysis, 120 Broadway, New York, has created an office of epidemic coordinator to insure maximum efficiency in meeting the challenge of poliomyelitis this summer. All epidemic activities of the national office will be channeled through the office of Epidemic Coordinator West J. Altenburg. He will be assisted by a committee: Dr. Hart E. Van Riper, Scarsdale, N. Y., medical director; Louis H. Haughey, comptroller, and George H. LaPorte, director of public relations. The epidemic coordinator's responsibility will be the speedy recognition of danger spots, correlation of information and of national office and field activities, and the evaluation of requests from the field to avoid duplication of effort. Equipment pools, each with respirators and hot pack machines, have been established by the foundation in Boston, Columbus, Ohio, and Des Moines, Iowa. Four epidemic aid teams, each consisting of an epidemiologist, orthopedist, pediatrician, an orthopedic nurse and two physical therapists, are ready to go into any epidemic area at the request of state health departments. The foundation reports that the country is better equipped to cope with infantile paralysis outbreaks than ever before and that cooperation between official and private agencies, state and county health departments, general hospitals, medical and nursing groups and the National Foundation has been improved.

International College of Surgeons.—The twelfth annual assembly and convocation of the United States chapter of the International College of Surgeons will meet September 28-October 4 at the Palmer House, Chicago, under the presidency of Dr. Herbert A. Acuff, Knoxville, Tenn. A combined operative and clinical program has been arranged. Besides numerous authorities, members of the United States chapter, the following visitors will be on the program: Dr. Hamilton Bailey, London, England; Dr. Raymond Darget, Bordeaux, France, "Treatment of Inveterate Cystitis by Infiltration of the Nervi Erigentes and Denervation of the Bladder"; Dr. Basil Hughes, Cornwall, England, "Lister's Conceptions and Those of Today"; Dr. William O. Lodge, Halifax, England, "Transantral Approach to the Gasserian Ganglion"; Dr. Felix Mandl, Jerusalem, Palestine, "Sympathetic Block in Sympathetic Surgery"; Dr. J. Almeida Rios, Rio de Janeiro, "Surgical Treatment of Osteomyelitis"; Dr. August Maria Sisson, Porto Alegre, Brazil, "New Technic to Produce Better Apical Collapse of the Lung"; Dr. Alex W. Spain, Dublin, Ireland, "Symphysiotomy in Modern Obstetrics."

On October 3 operative clinics, round table discussions and demonstrations will be held at Cook County Hospital under the direction of Dr. Karl A. Meyer, and clinics will be given October 4 at many Chicago hospitals. Dedication of the home of the United States chapter of the International College of Surgeons, the Blair mansion, 1516 Lake Shore Drive, purchased earlier this year, will take place at 8 p. m. October 2. The annual banquet will be held at the Palmer House at 6 o'clock October 1, and convocation will be at the Stevens Hotel, October 3, at 8 p. m. Reservations should be made promptly by writing Dr. Francis D. Wolfe, Chairman, Housing Committee, International College of Surgeons, % Chicago Convention Bureau, 33 North LaSalle Street, Chicago 2.

FOREIGN

Bubonic Plague in Haifa.—Palestine Senior Medical Officer Dr. James S. M. Pollock reported July 7 that bubonic plague had stricken 14 persons at Haifa. Antiplague measures launched by health authorities include a widespread rat extermination campaign, the spraying of infected areas with DDT and warnings to the population to take certain preventive measures.

Acta Urologica.—A new periodical under this title aims to publish special articles in the field of surgical urology and allied fields of medical science. It is a joint publication of the Clinic for Surgical Urology of the Pazmany Peter University of Budapest and the Publishing Company of the Free Union of the Hungarian Physicians and Surgeons. It will be published in English, French, Russian and German and will appear six times a year. The editors are A. Babics and E. Szold of Budapest, and on the board of collaborators are names from Vienna, Paris, Bern, Prague, Bratislava, Bucharest and Copenhagen.

CORRECTION

Postgraduate Courses for Practicing Physicians.—In the June 21 issue of THE JOURNAL, page 734, the second institution and course listed should read American College of Radiology, 20 North Wacker Drive, Chicago; at various cities during the year; radiology; one week; $50.

Marriages

GEORGE LEONARD EMMEL III, Gainesville, Fla., to Miss Rachel Bushnell Rodenbach of Naugatuck, Conn., March 29.

EVERT ALFRED LARSSON, Trenton, N. J., to Miss Torborg Margareta Eriksson in Lidköping, Sweden, February 9.

FRANCIS LEO MCNELIS, Pawtucket, R. I., to Miss Shirley Lucille Grube at Pocantico Hills, N. Y., June 21.

EUGENE B. MELINKOFF, Los Angeles, to Miss Beryl Cameron of San Francisco in Las Vegas, Nev., recently.

JOHN WESTON MANDEVILLE, Muskegon, Mich., to Miss Marilyn Ann Thomas of Detroit March 22.

LOGAN OLIVER JONES, Charlotte, N. C., to Miss Joan Duncan Shaw of Greenwich, Conn., March 15.

ALFRED E. GREENWALD, New York, to Miss Leatrice Joy Fleishman at Newark, N. J., June 15.

JOHN LEWIS READ, Camden, N. J., to Miss Dorothy Patricia Diana of Sharpsville, Pa., February 8.

JOHN C. MARKLEY, Georgetown, Ohio, to Miss Eleanore Dundon at Cincinnati February 15.

EDWIN S. OLSAN, Rochester, N. Y., to Miss Dorothy R. Dryfoos of New York January 23.

JOSEPH MARKEL, Staten Island, N. Y., to Miss Barbara Klauber of New York March 14.

JOHN EUGENE RAY to Miss Jane Rooks Tuttle, both of Humboldt, Tenn., Dec. 30, 1946.

VINCENZO R. ONORATO, Montclair, N. J., to Miss Ida Di Bella of Verona in February.

ROBERT HUGH MANHEIMER to Miss May Rosner, both of New York, March 2.

JACK H. LEVY, Newington, Conn., to Miss Beatrice Bogin at Hartford March 15.

WOODROW MILLER to Miss Joyce Lee Davidson, both of Los Angeles, recently.

Deaths

Thomas Martin Joyce ● Portland, Ore.; born in Emmetsburg, Iowa, Jan. 28, 1885; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1910; an intern and surgical assistant at St. Mary's Hospital, Rochester, Minn.; during World War I chief surgeon at Base Hospital number 46, serving with the American Expeditionary Forces; Kenneth A. J. Mackenzie professor of surgery and head of the department at the University of Oregon Medical School; chairman, Section on Surgery of the American Medical Association, 1939-1940; member of the founders group of the American Board of Surgery; formerly vice president of the American Association for the study of Goiter and the Pacific Coast Surgical Association; member of the American Surgical Association, Portland Academy of Medicine, Southern Surgical Association, North Pacific Surgical Association and the American Association for the Study of Trauma; fellow of the American College of Surgeons; attending surgeon at St. Vincent's Hospital; head of the department of surgery at the Portland Clinic and the Multnomah County Hospital, where he died April 18, aged 62, of coronary thrombosis.

Oscar Theodore Schultz, Evanston, Ill.; Johns Hopkins University School of Medicine, Baltimore, 1903; past president of the Illinois Society of Pathologists; member of the American Association of Pathologists and Bacteriologists; specialist certified by the American Board of Pathology; veteran of the Spanish-American War and World War I; for many years on the staff of the Michael Reese Hospital in Chicago and St. Francis Hospital; died in the Veterans Administration hospital March 7, aged 69, of acute cholangitis, miliary liver abscesses and old hemiplegia.

Virginia Pereira Alvarez-Hussey, Philadelphia; Woman's Medical College of Pennsylvania, Philadelphia, 1920; died in the Woman's Hospital April 12, aged 56, of malignant hypertension and cardiac decompensation.

Frank Leroy Andrews ● Chicago; Chicago College of Medicine and Surgery, 1916; on the staff of the Grant Hospital; died April 19, aged 61, of cerebral hemorrhage.

Harold Taylor Antrim ● Philadelphia; University of Pennsylvania School of Medicine, Philadelphia, 1917; served during World War I, as city police surgeon and on the staffs of the Episcopal Hospital and Stetson Hospital, where he died April 28, aged 54, of hemorrhage due to esophageal varices and portal cirrhosis.

Harry N. Asar ● Wheeling, W. Va.; Georgetown University School of Medicine, Washington, D. C., 1928; killed in an airplane accident near Moundsville April 20, aged 47.

Louise W. Beamis-Hood ● Buffalo; University of Buffalo School of Medicine, 1919; for many years secretary of the Medical Society of the County of Erie; served as president of the Women's Medical Society of the State of New York and as vice president of the Medical Women's National Association; died in the Buffalo General Hospital April 12, aged 68, of hypertension and myocardial infarction.

Robert L. Bean, Cleveland, Tenn.; Chattanooga Medical College, 1898; served on the county draft board during World War I; died April 19, aged 80, of myocarditis.

Jacob Andrew Bieri Jr., St. Louis; St. Louis University School of Medicine, 1930; member of the American Medical Association; formerly on the faculty of his alma mater; died in the Alexian Brothers Hospital April 12, aged 41, of cirrhosis of the liver and rheumatic heart disease.

Enos Hoyt Bigelow, Framingham, Mass.; Harvard Medical School, Boston, 1882; member of the American Medical Association; past president of the Massachusetts Medical Society and the Middlesex South District Medical Society; served in the state legislature; chairman of the board of health and the school committee; on the staff of Framingham Hospital; died March 13, aged 91, of arteriosclerosis.

Joseph Emanuel Blasenstein, New York; Columbia University College of Physicians and Surgeons, New York, 1920; specialist certified by the American Board of Pediatrics; for many years affiliated with the contagious disease division of the city health department; member of the staffs of the Sydenham and Morrisania hospitals; died April 3, aged 50, of coronary thrombosis.

Alta Emma Cullen Bordner, Duncan Okla.; Northwestern University Woman's Medical School, Chicago, 1892; for many years affiliated with the Colorado State Hospital in Pueblo, Colo.; died in the Lindley Hospital April 2, aged 72, of coronary thrombosis.

Joseph G. Bosley, Richmond, Ky.; University of Louisville Medical Department, 1892; served as county health officer; director of the Richmond Building and Loan Association; on the staffs of the Pattie A. Clay Infirmary and the Gibson Hospital where he died April 7, aged 79, following an operation for Hirschsprung disease.

Thomas McGrath Brennock ● Jersey City, N. J.; University of Pennsylvania Department of Medicine, Philadelphia, 1917; past president and secretary of the Hudson County Medical Society; fellow of the American College of Surgeons; diagnostician for the city board of health; served during World War I; affiliated with the Margaret Hague Hospital, Greenville Hospital, Fairmont Hospital and the Medical Center, where he was chief of the gynecologic service and where he died April 3, aged 55, of carcinoma of the bladder.

Alcus James Carter, Dayton, Texas; Tulane University of Louisiana School of Medicine, New Orleans, 1911; served as president of the Jones County (Miss.) Medical Society; formerly superintendent of the South Mississippi Charity Hospital, Laurel; died April 17, aged 64, of cerebral hemorrhage.

Crawford Haralson Cleveland ● Anniston, Ala.; Vanderbilt University School of Medicine, Nashville, Tenn., 1915; on the staff of the Anniston Memorial Hospital; president of the Y. M. C. A. board of directors; director of the Anniston Chamber of Commerce and the Commercial National Bank; died in Emory Hospital, Atlanta, April 2, aged 58, of glioblastoma.

Elmer Sherman Clouting ● Philadelphia; Jefferson Medical College of Philadelphia, 1896; affiliated with the Philadelphia General Hospital for many years; died in the Chestnut Hill Hospital April 29, aged 75, of nephritis and edema of the lungs.

John Andrew Collins ● Washington, D. C.; Washington University School of Medicine, St. Louis, 1902; fellow of the American College of Surgeons; member of the staff of the Episcopal Eye, Ear and Throat Hospital; died April 9, aged 69, of pulmonary edema.

Sidney James Colton ● Johnstown, N. Y.; University and Bellevue Hospital Medical College, New York, 1909; for many years public school physician; served on the staff of the Nathan Littauer Hospital in Gloversville; died April 8, aged 62, of coronary occlusion.

Percy Ray Cruse, Houston, Texas; Memphis (Tenn.) Hospital Medical College, 1912; member of the American Medical Association; chief consulting surgeon for the Burlington-Rock Island Railroad; died March 28, aged 59, of cerebral hemorrhage.

Hiram Day, Maryville, Mo; Ensworth Medical College, St. Joseph, 1892; served as county physician and as deputy state health commissioner; on the staff of St. Francis Hospital; died April 11, aged 78, of coronary sclerosis.

Frank K. Doane, St. Louis; St. Louis College of Physicians and Surgeons, 1905; served on the staffs of the Christian and St. John's hospitals; died April 27, aged 65, of heart disease.

John Donnelly, Charlotte, N. C.; University of North Carolina School of Medicine, 1905; member of the American Medical Association and the American College of Chest Physicians; past president of the Southern Sanatorium Association; served in France during World War I; formerly superintendent of the Mecklenburg Sanatorium in Huntersville; died April 9, aged 68, of cerebral hemorrhage.

Charles John Edwards, Vicksburg, Miss.; Medical Department of Tulane University of Louisiana, New Orleans, 1907; member of the American Medical Association and the American Academy of Ophthalmology and Otolaryngology; served during World War I; on the staff of the Vicksburg Hospital, Mercy Hospital and Vicksburg Infirmary; died March 13, aged 62, of coronary thrombosis, arteriosclerotic heart disease and chronic nephritis.

James Washington Ethridge, Lucy, Tenn.; University of Tennessee Medical Department, Nashville, 1899; served on the staffs of the Methodist, John Gaston, Baptist and St. Joseph's hospitals in Memphis; died April 14, aged 73, of heart disease.

Charles Israel Granstein, Chicopee, Mass.; Tufts College Medical School, Boston, 1910; died in the Mercy Hospital, Springfield, April 11, aged 59, of angina pectoris.

Leopold Sanford Gumberts ● Chicago; Jenner Medical College, Chicago, 1908; died April 27, aged 83, of chronic myocarditis.

Alpheus Tisdale Hafford ● Albion, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1913; fellow of the American College of Surgeons; city health officer; on the staff of the Sheldon Memorial Hospital; died in Battle Creek April 23, aged 57, of coronary thrombosis.

Emory Sylvester Hall ● McLeansboro, Ill.; Northwestern University Medical School, Chicago, 1908; served overseas during World War I; captain, medical reserve corps, not on active duty; owner of the McLeansboro Hospital; died April 4, aged 73, of coronary thrombosis.

Harold Charles Harpfer ● Wheeling, W. Va.; University of Pennsylvania School of Medicine, Philadelphia, 1926; member of the medical staffs of the Ohio Valley General and the Wheeling hospitals; died April 1, aged 46, of coronary thrombosis.

Eric Albert Hartley ● Chicago; Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin, Prussia, Germany, 1913; associated with the Columbus Hospital; served an internship and residency at the Knickerbocker Hospital in New York and the American Hospital in Chicago, where he died April 10, aged 59, of carcinoma.

William Davis Hawker, St. Louis; St. Louis University School of Medicine, 1911; member of the American Medical Association; died in the Deaconess Hospital April 3, aged 73, of septicemia.

Major Joel Henderson, Baker, Fla.; Rush Medical College, Chicago, 1937; died April 1, aged 38, of rheumatoid arthritis.

William Clarence Hess ● Cresco, Iowa; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1901; president of the Howard County Medical Society; president of the staff of the Mercy Hospital; died April 6, aged 72, of heart disease.

John Thomas Hickerson, Kansas City, Mo.; Marion-Sims College of Medicine, St. Louis, 1892; served during World War I; died March 10, aged 80.

William A. Hillemeyer ● Chicago; Jefferson Medical College of Philadelphia, 1896; member of the staff of the Woodlawn Hospital; died April 5, aged 71, of coronary occlusion.

James Arthur Holley, Walton, N. Y.; Albany Medical College, 1886; member of the American Medical Association; died April 20, aged 92, of heart disease.

Irving Woodward Hollingshead ● Philadelphia; University of Pennsylvania Department of Medicine, Philadelphia, 1894; on the staff of the Methodist Hospital, where he died April 23, aged 75, of pneumonia.

Harwood Leroy Hollis ● Lacona, N. Y.; Syracuse University College of Medicine, 1920; past president of the Oswego County Medical Society; fellow of the American College of Chest Physicians and the American Trudeau Society; member of the village board; formerly a member of the board of education of Sandy Creek High School; served as president of the First National Bank of Lacona; superintendent of the Oswego County Sanatorium in Richland; died April 28, aged 52, of coronary thrombosis.

Thomas Jefferson Houston, Meridian, Miss.; University of Tennessee Medical Department, Nashville, 1889; served during World War I; formerly city health officer; at one time on the faculty of the Mississippi Medical College; died April 18, aged 81.

George Stem Hullich, Aldan, Pa.; Hahnemann Medical College and Hospital of Philadelphia, 1943; member of the American Medical Association; interned at the Hahnemann Hospital; served during World War II; was accidentally shot and killed March 29, aged 30, while cleaning a pistol.

William Otis Hunt, North Falmouth, Mass.; Harvard Medical School, Boston, 1877; member of the American Medical Association; for many years on the staff of the Newton (Mass.) Hospital; died in Wiscasset, Maine, April 19, aged 92, of cerebral hemorrhage.

Adolph Xavier Kamm, Ashland, Wis.; the Hahnemann Medical College and Hospital, Chicago, 1918; member of the American Medical Association; on the staff of St. Joseph's Hospital; died March 30, aged 57, of coronary occlusion.

Herbert Weaver Kendell ● Covington, Ohio; Ohio Medical University, Columbus, 1898; for many years member of the board of education, director and president of the Covington Building and Loan Company; served on the staff of the Piqua (Ohio) Memorial Hospital; died March 16, aged 71, of cerebral hemorrhage.

Harriet Ann Knott, Saginaw, Mich.; New York Medical College and Hospital for Women, Homeopathic, New York, 1894; died in Midland March 17, aged 79, of pneumonia.

George Abraham Lassman ● New York; College of Physicians and Surgeons, Baltimore, 1906; member of the American College of Chest Physicians; died April 3, aged 63, of heart disease.

Isidor Morris Lavine ● Mount Rainier, Md.; George Washington University School of Medicine, Washington, D. C., 1941; also a lawyer; diplomate of the National Board of Medical Examiners; interned at the Gallinger Municipal Hospital in Washington, D. C.; affiliated with the Prince Georges' General Hospital, Cheverly, where he was secretary of the staff; on the staffs of the Sibley and Children's hospitals in Washington, D. C.; died April 5, aged 42, of coronary occlusion.

Edward McCrady L'Engle, Jacksonville, Fla.; Johns Hopkins University School of Medicine, Baltimore, 1902; served as secretary-treasurer of the Florida Public Health Association; for many years director of the bureau of vital statistics and formerly member of the state board of health; for many years trustee of the city public library and president of the board of directors of St. Luke's Hospital; died April 19, aged 68, of cerebral hemorrhage.

Isaac Richard Le Sage, Huntington, W. Va.; Medical College of Ohio, Cincinnati, 1888; died April 30, aged 81.

Frank Liberson, New York; Long Island College Hospital, Brooklyn, 1917; specialist certified by the American Board of Radiology; member of the American College of Radiology; served with the U. S. Public Health Service; roentgenologist at the radiologic clinic at U. S. Marine Hospital number 13 on Staten Island; died April 16, aged 58, of coronary occlusion.

Walter Linebeck, La Belle, Fla.; Cincinnati College of Medicine and Surgery, 1897; died March 27, aged 79, of acute dilatation of the heart.

Walter M. McGaughey ● Greencastle, Ind.; Medical College of Indiana, Indianapolis, 1902; county and city health officer; veteran of the Spanish-American War; surgeon for the New York Central and Pennsylvania Railroad; died March 24, aged 75, of coronary disease.

John Malcolm Maples, Florence, Ala.; University of Louisville (Ky.) School of Medicine, 1907; member of the American Medical Association; died in Selma March 21, aged 74, of coronary thrombosis.

Milton Leon Mooney, Mountain Home, Ark.; College of Physicians and Surgeons, Little Rock, 1907; served as health officer of Baxter County; died April 1, aged 70, of cerebral hemorrhage.

Howard Delano Moore, Danbury, Conn.; Hahnemann Medical College and Hospital of Philadelphia, 1893; member of the American Medical Association; served on the staff of the Danbury Hospital; died March 28, aged 79, of gangrene of the foot, diabetes mellitus and general arteriosclerosis.

Carroll Hampton Morgan, Memphis, Tenn.; Chattanooga Medical College, 1910; member of the American Medical Association; died in the Baptist Hospital March 29, aged 60 of cerebral hemorrhage.

Joseph Mack, Kew Gardens, N. Y.; University and Bellevue Hospital Medical College, New York, 1911; served on the staff of the Harlem Hospital in New York; died in February, aged 57.

Andrew Nagy, West Los Angeles, Calif.; Magyar Királyi Pázmány Petrus Tudományegyetem Orvosi Fakultása, Budapest, Hungary, 1927; died in Santa Monica March 1, aged 46, of myocardial infarction and arteriosclerosis.

Lorenzo Bowen Phillips ● Inwood, N. Y.; University of Pennsylvania Department of Medicine, Philadelphia, 1895; for many years affiliated with St. Joseph's Hospital in Far Rockaway; died March 31, aged 82, of coronary thrombosis.

Elbridge Worthington Pierce, Meriden, Conn.; University of the City of New York Medical Department, New York, 1885; president emeritus of the Meriden Hospital; died April 4, aged 84, of arteriosclerotic heart disease.

Joseph Pore ● Ambridge, Pa.; Maryland Medical College, Baltimore, 1911; also a pharmacist; member of the American Heart Association; examining physician, Beaver County Local Board number 6, Selective Service System; medical examiner for the local school system; served on the staffs of St. Elizabeth Hospital in Youngstown, Ohio, and the Sewickley Valley (Pa.) Hospital; died in the Mercy Hospital, Pittsburgh, April 27, aged 64, of carcinoma of the lung.

George Thomas Pruitt, Meridian, Miss.; Memphis (Tenn.) Hospital Medical College, 1912; died March 20, aged 73, of coronary thrombosis.

George William Pugsley ● Bayard, Neb.; John A. Creighton Medical College, Omaha, 1907; an officer in the medical corps of the U. S. Army during World War I; for many years councilor of the Twelfth District of the Nebraska State Medical Association; died March 23, aged 66, following an automobile accident.

Thomas Everette Romine, Charleston, W. Va.; University of Louisville (Ky.) School of Medicine, 1911; died March 28, aged 60, of a skull fracture received when struck by an automobile.

Benjamin Clark Sawyer, Darlington, Pa.; Medical Department of the Western University of Pennsylvania, Pittsburgh, 1903; member of the board of education; died March 2, aged 70, of cardiovascular renal disease.

Richard Frederick Schiele ● Glen Ellyn, Ill.; University of Illinois College of Medicine, Chicago, 1915; died April 9, aged 55.

George Winthrop Shoemaker, Syracuse, N. Y.; Syracuse University College of Medicine, 1897; one of the founders of the Onondaga General and People's hospitals; died March 29, aged 84, of myocarditis.

Shelby Epler Stinnette ● St. Paul; the Hahnemann Medical College and Hospital, Chicago, 1913; affiliated with Midway, Mounds Park and Bethesda hospitals; died in Los Angeles March 27, aged 60, of coronary thrombosis and hypertension.

Fred Foster Stocking, Fargo, N. D.; Rush Medical College, Chicago, 1906; member of the American Medical Association and the Minnesota State Medical Association; fellow of the American College of Surgeons; served overseas during World War I; chief rating officer at the Veterans Hospital; died in April, aged 67.

Frank Austin Toepell, Russell, N. Y.; University and Bellevue Hospital Medical College, New York, 1899; member of the American Medical Association; served as health officer; died recently aged 76.

William Scott Tinney Sr., Strasburg, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1903; member of the American Medical Association; served as coroner and physician for the board of health; died March 21, aged 67, of angina pectoris.

Karl Rand Tuttle, Haverhill, Mass.; Dartmouth Medical School, Hanover, N. H., 1888; died March 28, aged 86, of myocarditis and arteriosclerosis.

Pitt Abraham Wade, Canon City, Colo.; Barnes Medical College, St. Louis, in 1898 and 1899; died in National City, Calif., March 19, aged 77, of carcinoma of the prostate.

Jacob R. Wiggers, Grand Rapids, Mich.; Ohio State University College of Homeopathic Medicine, Columbus, 1917; member of the American Medical Association; died March 22, aged 61, of coronary thrombosis.

Thomas Marion Williams, Palo Alto, Calif.; Columbia University College of Physicians and Surgeons, New York, 1901; served in the U. S. Navy during World War I; formerly member of the city council; served as health officer of Palo Alto, medical adviser for Stanford University and special consultant in surgery at the Men's Student Health Service; for many years chairman of the Stanford Board of Athletic Control; affiliated with the Palo Alto Hospital; died March 26, aged 76, of cerebral hemorrhage.

Lieut. (jg) Ford P. Eshleman Jr. (MC), U. S. N. R., 1919-1945

Capt. Ralph C. Berkelhamer M. C., A. U. S., 1914-1944

Capt. John S. Doherty M. C., A. U. S., 1914-1945

Henry Edward Stone, Boston; Tufts College Medical School, Boston, 1912; member of the American Medical Association; interned at the Lynn (Mass.) Hospital; died in Miami Beach, Fla., March 31, aged 57, of coronary thrombosis.

KILLED IN ACTION

Ford Powell Eshleman Jr., Lakemills, Wis.; Northwestern University Medical School, Chicago, 1943; interned at the St. Luke's Hospital in Chicago, where he served a residency; began active duty in the medical corps of the U. S. Naval Reserve as a lieutenant (jg) on Oct. 10, 1944; began sea duty as ship's surgeon on the U. S. S. *Napa* which landed Fourth Division Marines on Iwo Jima on D-Day; aboard the U. S. S. *Braine* which was on patrol duty from Leyte to Okinawa and was attacked by enemy suicide planes off the east coast of Okinawa on May 27, 1945, aged 26; declared dead Oct. 5, 1945.

Ralph Carl Berkelhamer, Chicago; University of Illinois College of Medicine, Chicago, 1939; interned at the Englewood Hospital and the Cook County Hospital, where he served a residency; began active duty as a first lieutenant in the medical corps, Army of the United States, in May 1941; promoted to captain; prisoner on Bataan, where he survived the "Death March"; detachment commander at the hospital unit at Prison Camp Number 1 at Cabanatuan; awarded Silver Star for gallantry in action on Bataan and Bronze Star for excellent service while in prison camp; killed in action in the South China Sea Oct. 24, 1944, aged 30, when the ship on which he was being transported was sunk.

John Stephen Doherty, Lockport, N. Y.; University of Buffalo School of Medicine, 1941; diplomate of the National Board of Medical Examiners; interned at the Buffalo Hospital of the Sisters of Charity; began active duty as a first lieutenant in the medical corps, Army of the United States, on Aug. 18, 1942; promoted to captain; battalion surgeon of the 319th Glider Field Artillery; missing in action in Holland on Sept. 18, 1944; declared dead Sept. 19, 1945 by the War Department, aged 31.

Foreign Letters

LONDON

(From Our Regular Correspondent)

June 7, 1947.

Alleged Injury to Workers at an Atomic Research Station

It is alleged that workers in an atomic research center in England have developed symptoms arising from their employment. This claim is made in the daily press by the assistant general secretary of the Chemical Workers Union. Among the symptoms enumerated are lassitude, skin eruptions and impotence. Of 250 men working at the plant he states that 20 complain of impotence. This allegation is being investigated by the inspectors of the Ministry of Labor. At the same time a spokesman of the Ministry of Supply has stated that the only instance of disorder due to radioactivity in this and other plants is 1 case of dermatitis. Also Professor N. F. Mott, president of the Atomic Scientists Association, has stated that the methods of protection are so easily applied and so strictly enforced that it is inconceivable that workers could be affected. The impotence and sterility of which radar workers complained during the war were apparently not of occupational origin. It has to be remembered that, with a labor government in control of the country, workers have every opportunity to exploit real or alleged grievances.

Army Memorial to Help the Living

The Royal Army Medical Corps War Memorial Fund, for which $36,000 has been raised within the corps itself, has been commended to a wider public by Lieut. Gen. Sir Alexander Hood, director general of the army medical services. It is proposed to spend the fund mainly for the living rather than set up an expensive monument. This decision was taken by a large meeting representative of all ranks and all types of service. The fund will therefore be devoted first to the welfare of families of all ranks of the corps who fell in the war; also of all ranks who served in the war, and of their families, who may be in need through sickness or other misfortune. The intention is not to build up any large capital sum but to give substantial help where necessary. It is expected that the fund will be all distributed in some six or seven years.

At a press reception held at the headquarters of the corps Sir Alexander Hood made a threefold appeal for support of the fund: to his comrades of all ranks of the corps, to physicians in civil life, and to other arms and services and the general public. He felt that among the many thousands who passed, sick or wounded, through the medical units there were many who would like to take this opportunity of paying a practical tribute to those who looked after them in desert, jungle, prison camp, and every theater of war.

Artificial Insemination: Moral and Legal Objections

It is only recently that the question of artificial human insemination has attracted attention in this country. A conference on the subject has been held in London under the auspices of the Public Morality Council. The subject was discussed from every point of view by speakers representing the medical profession, the churches and the law. The problem was outlined by Dr. H. P. Newsholme, health officer of Birmingham. In the artificial insemination of a wife with her husband's semen he objected to obtaining the semen by masturbation as a lowering of human dignity. The only legitimate method was insemination from the vaginal pool after normal coitus. Mr. Kenneth Walker, a neurologist, who is an expert in male fertility, dealt with the use of donated semen. He had seen many more marriages saved rather than wrecked by this procedure. The theological aspect was dealt with by speakers representing the Roman Catholic Church, the Church of England and the Free Churches. Rev. J. C. Heenan, D.D., speaking for the Roman Catholic Church, condemned artificial birth prevention as "masturbation *à deux* and morally wrong. It was not only permissible but extremely desirable that marital intercourse, for some reason unfruitful, should be perfected by medical skill. This might take the form of preparing the vagina beforehand in order to overcome some obstacle or intervention after normal intercourse to assist the deposited seed toward its natural objective. But artificial fecundation properly so called was unlawful. Artificial insemination from a donor was revolting. For the Church of England Rev. G. L. Russell, a physician also, said that for insemination of a wife there was no practical alternative to masturbation and he did not believe that on moral grounds this should be prohibited. But, like all the clerical speakers, he regarded the use of donor's semen as morally objectionable.

A lawyer, Mr. J. P. Ashworth, saw great legal difficulties in the use of donor semen. If pregnancy followed and the mother registered the child as her husband's she would be guilty of perjury. Also the child would be illegitimate. Legacies to the child in the belief that it was legitimate would be invalidated. Then there was the danger that children of the same father, ignorant of the fact, might marry and so be guilty of incest.

The case for artificial insemination was stated by two women doctors. Dr. Mary Barton said that artificial insemination had been a portion of her daily practice for five years. About 10 per cent of marriages were sterile, and in about 60 per cent of these the male was affected. In about 3 per cent he was hopelessly sterile. There was no greater disruptive element in married life than a fertile woman living with a man who could never give her a child. There was no stronger urge in the developed woman than the bearing of children. Adoption of children was a solution in only a minority of cases. In arranging for a donor of semen it was insisted that the matter should remain a secret. Appalling damage might be done to the child by the discovery that the man reputed to be its father was actually not. In an experience of 300 donor cases the results had been satisfactory. The children were healthy and the woman and her husband had been happy.

Paraplegia Following Spinal Anesthesia: Damages for Negligence Against the Hospital Authorities

The disastrous effect of a spinal anesthetic has led to legal proceedings in which heavy damages for negligence were awarded against the hospital authorities but not against the medical staff responsible for the operation—a most unusual difference in such cases. A boy fractured his femur while playing football and was taken to a hospital at Portsmouth. In order to reduce the fracture a spinal injection of nupercaine was given in the ward, not in the operating room. Some days later meningitis was diagnosed, which was found to be due to infection with Pseudomonas aeruginosa. The result was that the boy became permanently paraplegic and could not retain his urine. In the action for damages three members of the medical staff of the hospital, including the orthopedic surgeon, were cited as defendants with the hospital authority. The judge found no evidence of any negligence on their part in the treatment of the fracture, the decision to administer a spinal anesthetic, the doing so in the ward instead of the operating room, or in treating the patient after the meningitis was diagnosed. He was satisfied that the skin was properly cleansed before the operation and that the operator had prepared himself in the approved way. The only remaining source of infection was the apparatus, for which the nursing staff was responsible. The infection could not have arisen without negligence on the part of the hospital service. He accordingly

gave judgment in favor of the medical staff but against the hospital authorities. For the terrible disability of the boy, for which no money could compensate, he awarded $48,000 damages with costs. Notice of appeal against this judgment was lodged.

ANKARA

(From Our Regular Correspondent)

May 22, 1947.

Outbreak of Bubonic Plague

In March and April this year an outbreak of bubonic plague, of which Turkey had been free for a number of years, was reported from the southern frontiers of Urfa, where it was confined to three villages. The Ministry of Health immediately rushed by airplane the necessary equipment for preventive and curative measures to the infected areas. The frontiers were immediately closed and put under strict quarantine. The whole population of all southern provinces was vaccinated. All means of transportation were inspected and disinfected. Day and night almost two hundred persons (the director general of hygiene, 1 specialist, 1 bacteriologist, 1 district health officer, 68 health officers and physicians, 75 sanitary inspectors and 53 sanitary agents) were engaged in the work and two mobile hospitals and one mobile laboratory were used for the destruction of rats, mice, vermin and insects. Five and one-half tons of DDT, 201 tons of gasoline and 191 tons of benzine were employed. There have been 18 cases and 13 deaths and on April 9 the outbreak was considered closed. It has been revealed that the disease came in from Syria, where it is sometimes sporadic among desert nomads along the frontier and where no serious attempts had been made to prevent its spread. In the infected frontier villages only a few dead rats were found infected with Bacillus pestis.

The vigil along the frontier has not been abandoned, especially as recently 6 new cases of bubonic plague have been reported from the Syrian village of Varta. All arrivals from Syria must submit to close examination. The Central Institute of Health has provided the southern provinces with a generous supply of vaccine and serum. The outbreak has been reported in full detail to the Interim Commission of the World Health Organization at Geneva.

The Shortage of Trained Nurses

In 1942 the Turkish Red Crescent Society in Istanbul opened the first nursing school in Turkey. An eighth grade school certificate was required for admission to the competitive entrance examination. No fees were charged for tuition, board, maintenance and uniforms. The course was three years and a diploma was given. After graduation a five years compulsory service was required, and marriage during this period was not permitted. Noncompliance obligated the student to repay the expenses incurred in her training. At its inception the school had many applications and had from thirty to forty graduates each year. Most of the theoretical instruction was given by physicians and foreign trained nurses; for practical experience the students were sent to government and city hospitals. Graduates were given positions at governmental general hospitals. After several years of satisfactory work these nurses advanced to the position of head nurse.

With the advent of the republic, the reorganization of hospitals and the extension of health activities, it became increasingly evident that the number of graduates from this one school was wholly inadequate to meet the demand, especially as since the beginning of the last war the number of applications decreased and students began to leave after the probationary period. Less than a hundred students have graduated from the school so far. Bedside nursing at nearly all hospitals is still mostly done by practical nurses, who after a certain time and if their work has been satisfactory take an examination; having satisfied the board of examiners, they receive a certificate and an increase in pay, but they never attain the status of a trained nurse. In male wards and dermatologic clinics male nurses are employed. At present the place of the trained nurse in many general and maternity hospitals is taken by the trained midwife, of which there is no shortage.

There are at present four schools of nursing in Turkey. One, the Red Crescent School of nursing in Istanbul, with an enrolment of almost a hundred students and under the direction of two American trained nurses, and the two schools of nursing established last year in Istanbul by the Ministry of Health, one in affiliation with the Haydar Pasha Model Hospital, the other in affiliation with the Children's Hospital and an enrolment of almost a hundred students. In addition to free tuition, board, maintenance and uniforms, the students receive a monthly allowance of 30 liras a month. Theoretical instruction is given by the medical staff of the respective hospitals. The graduates are required to give five years of compulsory service at governmental hospitals for expenses incurred in their training. At the head of these schools are two Turkish trained nurses who had several years of postgraduate work and study in the United States. The funds for the administration of these schools come from the budget of the Ministry of Health. To procure trained nurses for army hospitals the Army School of Nursing, with an enrolment of almost a hundred students, was opened at the beginning of the war at the Gülhane Military Hospital in Ankara. The requirements for admission and the educational program are the same as in the other schools, but in addition to a small allowance the students receive officer's food rations, but the obligatory service is ten years instead of five. The Turkish Child Welfare Society of Ankara has a foundling home with three hundred inmates, to which is attached a school for the training of children's nurses. The course is two years and the graduates are given positions at the many branch homes the society has in all parts of the country.

Last September the cornerstone was laid at Ankara for a 200 bed Red Crescent hospital in affiliation with a second Red Crescent School of Nursing for 200 students. The plans for the hospital and school were drafted by the French architect Jean Walter, who has also prepared the plans for the medical center now under construction in Ankara. The Red Crescent Hospital and School are expected to be finished by the end of next year.

There are also plans for the systematic training of male nurses. The number of trained nurses in Turkey is at present 457; of practical nurses, 631.

The inadequate supply of trained nurses for hospital and public health work will probably continue to be a problem for some time. The emancipation of women must also be regarded as a contributing factor to the shortage. Most girls with a higher education now enter professions that were formerly not open to them, and the continually growing school population also demands more and more teachers for all grades. To attract more desirable candidates to the nursing profession a law was passed in 1945 according to which trained nurses in government service who had already attained civil servant status in 1926 were promoted to a higher salary class. Under the 1945 law they are eligible for a pension.

School of Hygiene Renews Courses

With twenty physicians from different provinces, the School of Hygiene at Ankara, which in 1941 discontinued courses on account of war conditions, has recently renewed courses. Health officers, physicians engaged in antimalarial work and physicians engaged in work at health centers are taking a four months theoretical and practical course in preventive medicine, epidemiology, vital statistics, general, social, industrial and rural

hygiene, microbiology, malaria control work and sanitary engineering. The instructors are specialists from the Ministry of Health and Social Assistance and from Rockefeller fellows who did graduate work in preventive medicine in the United States. Field work is being done at the Etimesut Health Center, the Central Institute of Hygiene, the Ankara Model Hospital and the Malaria Prevention Center. For the small number of participants and the short duration of the course, postwar conditions and the continuing mobilization are responsible. It is hoped that a course of longer duration with more participants from remote provinces may be given next fall. The present course aims to prepare physicians so they will be able to direct the health centers that are to be opened in the near future.

BRAZIL

(From Our Regular Correspondent)

RIO DE JANEIRO, May 15, 1947.

Protection of the Liver and the Kidneys

Dr. Carlo Foa, professor at the University of Milan, Italy, has published his experimental studies performed at the Institute of Physiology of São Paulo, where he is a guest professor, on the protection of the liver and the kidneys by the synergic action of disintoxicating and lipotropic factors. The aim of Dr. Foa's studies was to compare the lipotropic power of choline with that of an enzymatic proteolysate of casein containing methionine, the antihepatosteatosis factors extracted from the pancreas, and the lipotropic and antinecrotic factors from an integral proteolysate of liver. He studied the separate action of each factor and also the simultaneous interaction of all of them.

As a fundamental alipotropic diet Dr. Foa used what he called diet A, containing casein 5 per cent, peanut flour 20 per cent, lard 20 per cent, starch 20 per cent, saccharose 28 per cent, agar 2 per cent, yeast 2 per cent, cod liver oil 2 per cent and Hawk and Oser's salt mixture 1 per cent. Rats fed on diet A showed a slow increase in weight and an extensive loss of hair, particularly of the head and sides. Several of these animals died on about the sixtieth day of the experiment from hepatic and renal disturbances caused by the diet. The postmortem examination of the liver disclosed steatosis with a variable distribution of fat. The most striking changes were present in the cells bordering the acinus near the periportal conjunctive tissue. Fat was seldom found in the central part of the lobuli but frequently in the intermediate zone. In some animals the most important changes were found around the central vein; in some others the fatty degeneration was mostly in the intermediate zone of the acinus, while its central part showed only necrobiotic lesions. A third group of animals presented fatty degeneration of the central part associated with severe necrosis of the intermediate zone. In many cases these diverse pictures were simultaneously found in different zones of the liver of the same animal, with fatty infiltration of the periphery of the acinus besides zones of necrosis and fatty degeneration of the central part. The infiltrated zones always presented the phenomenon of birefringence, the lipids, free or included in Kupffer's cells, being as a rule anisotropic. In some cases also the crystalline formations presented the anisotropic condition. Some rats were also fed on diets called B, C and D, the first containing 20 mg. of choline per day, the second containing the same amount of choline plus 20 mg. of inositol per day and the third one containing 20 mg. of choline and 20 mg. of the antihepatosteatosis factor extracted by the method proposed by Entenman, Montgomery and Chaikoff.

The average weight percentage of lipids of the liver of a lot of 10 rats fed on diet A was 22.65, while the same average for similar lots of animals fed on diets B, C and D was respectively only 9.70, 7.22 and 4.80. These results, in coincidence with the findings of microscopic examinations, demonstrated that the improvement caused by the lipotropic factors under study is more extensive when they act synergically, with great influence on the increase in weight, the growth of hair and the lipid content of the liver. Dr. Foa's conclusion is that choline, fed to rats showing definite liver steatosis caused by alipotropic diets without methionine, presents a high lipotropic power, which is increased by the synergic action of inositol. The action of these two factors is still greater when potentiated by the addition of the antihepatoesteatosis factor of Entenman, Montgomery and Chaikoff.

Chemistry of Normal Blood of Adults

Drs. Mario P. de Mesquita and Vera L. Ribeiro of the Fernandes Figueira Hospital of Rio de Janeiro have been studying for a number of years the blood chemistry of normal adults. Several of their studies have been reported in previous letters (hemoglobin, calcium, urea). The same authors have now published a report of their investigations on the normal content of uric acid in the blood, including 201 determinations, 152 in male persons and 49 in female persons. The variation of the value in males was minimum 1.6 mg., maximum 5.1 mg., mean 3.44 mg., standard deviation 0.61 mg.; in females minimum 1.6 mg., maximum 4.4 mg., mean 2.83 mg., standard deviation 0.65 mg. The mean value for the 152 males is 3.5 practically identical in all age groups.

The Antireticular Cytotoxic Serum

Drs. Eimar Povoa and Walter Guerreiro have reported the results of their first experimental work on the effects of the Bogomolets antireticular cytotoxic serum. After two years of hard work they succeeded in preparing the antireticular human serum, using spleen and bone marrow taken from a man free from infection and from cancer a few hours after his death. Using a technic similar to that of the preparation of rabbit serum against guinea pig and sheep serum against rabbit, they obtained a serum of low hemolytic power and with a high titer, which was employed in several human cases with partially good results. The present paper is a preliminary report.

Death of Dr. R. Leitão da Cunha

Dr. R. Leitão da Cunha, president emeritus of the Rio de Janeiro University, died recently at the age of 67. Graduating in 1902 from the Rio de Janeiro Medical School, Dr. Leitão da Cunha studied for some time in Europe. Returning to Brazil he was appointed professor of pathology at the Rio de Janeiro University and some time later was chosen to be president of the university. During a few years he was commissioner of health for the Federal District. He published several textbooks of medicine, among which was one on clinical pathology, which had a large use in Brazil. Two years ago he retired from active service, receiving the title of president emeritus of the university.

Brief Items

Dr. Arnaldo de Moraes, professor of clinical gynecology, University of Rio de Janeiro, has been elected corresponding member of the Société française de gynécologie. At the same time Dr. Moraes has been invited to be present at the eleventh French Congress of Gynecology, to be held this month at Chatel Guyon, France.

Dr. Amadeu Fialho, pathologist of the National Department of Health, has been appointed professor of pathology at the University of Rio de Janeiro, succeeding Dr. Paul Leitão da Cunha, who died a few weeks ago. Dr. Fialho, a leading specialist, is well known throughout the country. He is the author of many valuable papers.

Dr. C. Goulart de Andrade has been elected president of the Brazilian Association of Obstetrics and Gynecology. Dr. Andrade is assistant professor of obstetrics at the University of Rio de Janeiro.

Correspondence

THE THYROID GLAND

To the Editor:—I had the good fortune many years ago to be able to point out the dominating role of the thyroid gland in the production of energy. To the present day I am still surprised at the favorable reception which that research received and to find from time to time my name mentioned along with others to whom, in my opinion, science is indebted for the truly great discoveries in endocrinology. Those men had a creative insight and imagination for the solution of their problems involving the discovery of new resources and methods, both chemical and surgical. Nothing like this was requisite for my task. The problem presented itself to me almost of its own accord. Friedrich Mueller (*Deutsches Arch. f. klin. Med.* 51:335, 1893) was the first, in 1892, to draw attention to the altered protein metabolism in hyperthyroidism. Thereupon Leichtenstern and Murray (*Deutsche med. Wchnschr.*, 1894, No. 50) independently in 1893 inferred from purely clinical observation that the loss of weight resulting in obese patients from thyroid feeding must be due in part to combustion of their accumulated fat and thus yield an increased energy production. At that time I carried Mering and Zuntz respiration apparatus to the bedside of the patient. There was nothing more to do than to examine the gaseous metabolism in hyperthyroidism and in myxedema (Magnus-Levy, Adolph: *Berl. klin. Wchnschr.*, 1895, No. 30; *Ztschr. f. klin. Med.*, 1897, Nos. 3/4), a task which was accomplished in less than three years.

Fifty years have elapsed, and only now do I believe myself in a position to interpret the favorable reception accorded to these studies. Their success may have depended on the great simplicity of the question as formulated, as well as on the method employed for its answer. In addition it may be due to the circumstance that the problem was solved once and for all exclusively within the domain of human pathology.

I desire to express my deep felt gratitude to my American friends, who chiefly because of it invited me to New Haven and provided me, a stranger in a strange land, with a sheltering roof for the pursuits of my old age.

ADOLPH MAGNUS-LEVY, M.D., New York.

RHEUMATIC PNEUMONITIS

To the Editor:—Dr. G. C. Griffith in his article on "Rheumatic Fever" (THE JOURNAL, April 5, p. 974) appears to consider that rheumatic pneumonitis was first described in 1927. This is not so, for I referred to it in my "Manual of Children's Diseases," which was first published in 1905. One review severely criticized my statements, but since then I find that this type of pneumonia is now well recognized both in Great Britain and in America. Let me quote my original reference to it: "It may be also . . . that pneumonia may occasionally be caused by the specific organism of rheumatism." I agree with Dr. Griffith that subcutaneous nodules are not necessarily a grave prognostic sign. I stated in my book that I had "on several occasions met with rheumatic nodules where the patient was not very seriously affected and made a rapid and good recovery." Again, I state that "appendicitis is undoubtedly a rheumatic affection in not a few cases." I consider it a mistake to give sodium bicarbonate along with sodium salicylate or acetylsalicylic acid. As a rule too the doses given are inadequate. In cases of acute rheumatism doses much beyond the average are well tolerated and yield better results.

JAMES BURNET, M.D.,
14, Cumin Place,
Edinburgh, 9, Scotland.

CANCER TREATMENT BY AUTOVACCINATION

To the Editor:—In the correspondence on "Cancer Treatment by Autovaccination" in THE JOURNAL, March 15 and May 10, no mention is made of the significant work by Thomas Lumsden between the years 1925 and 1936. The fundamental work is reviewed in the *American Journal of Cancer* 15:563, 1931; the most recent paper in the series is in the same journal 33:395, 1938.

Since 1929, when Woglom published his somewhat overcritical review of tumor immunity (*Cancer Rev.* 4:129, 1929) the scientific atmosphere has been hostile to the subject of tumor immunity, and possibly valuable experimental work has been rejected on insufficient evidence. Lumsden's experiment on autovaccination in the treatment of transplanted tumors was apparently conclusive. In one especially significant experiment he studied a large group of animals which had sarcomas implanted on both hind legs. By injecting repeated small doses of formaldehyde into one tumor in each rat he was able to bring about a slow regression of the injected tumor. In a very large percentage of the treated animals the uninjected tumor also regressed so that both tumors were ultimately entirely destroyed. A comparison with control uninjected tumor bearing animals showed that the result was significantly due to the treatment employed. In subsequent work Lumsden carried out a careful analysis of the mechanism of this phenomenon and showed that it involved an autoimmunization with the formation of cytotoxic antitumor antibodies.

This important critical and imaginative research seems to have been overlooked by most investigators in the field.

ARTHUR SHAPIRO, M.D., Brooklyn.

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

BOARDS OF MEDICAL EXAMINERS
BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Examinations of the boards of medical examiners and boards of examiners in the basic sciences were published in THE JOURNAL July 12, page 976.

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: *Parts I and II.* Various centers, Sept. 15-17. *Part III.* Durham, Oct. 21-23. Sec., Mr. Everett S. Elwood, 225 S. 15th St., Philadelphia 2.

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF ANESTHESIOLOGY: Part II. *Oral.* Cleveland, Oct. 5-11. Sec., Dr. P. M. Wood, 745 Fifth Ave., New York 22.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY: *Part I. Oral.* Chicago, Oct. 24-26. Final date for filing application is Aug. 1. *Part II. Written.* Various centers, Sept. 15. Sec., Dr. C. M. Lewis, 66 E. 66th St., New York 21.

AMERICAN BOARD OF INTERNAL MEDICINE: *Oral.* Chicago, Oct. 8-10. Asst. Sec., Dr. W. A. Worrell, 1 West Main St., Madison 3.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: *Oral.* Chicago, May or June. Final date for filing application is Feb. 1. Sec., Dr. W. J. Germon, 310 Cedar St., New Haven, Conn.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Part I. Written.* Various Centers, Feb. 6. Final date for filing application is Nov. 1. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh 6.

AMERICAN BOARD OF OPHTHALMOLOGY: Chicago, October 6-12. Sec., Dr. S. Judd Beach, 704 Congress St., Portland, Me.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: Part II. Chicago, Jan. 22-23. Final date for filing application is Sept. 15. Sec., Col. F. H. McKenney, 1134 W. Sixth St., Los Angeles 14.

AMERICAN BOARD OF OTOLARYNGOLOGY: Chicago, Oct. 7-11. Sec., Dr. D. M. Lierle, University Hospitals, Iowa City, Ia.

AMERICAN BOARD OF PATHOLOGY: Chicago, Oct. 24-25. Final date for filing application is Sept. 15. Sec., Dr. Robert A. Moore, Euclid Ave. and Kingshighway, St. Louis 10.

AMERICAN BOARD OF PEDIATRICS: Dallas, Dec. 5-7. Philadelphia, Jan. 9-11. Sec., Dr. Lee F. Hill, 718 Royal Union Bldg., Des Moines 9.

AMERICAN BOARD OF PLASTIC SURGERY: Examinations are given in April and November of each year in the larger town of applicants. Applications should be sent to Sec., Dr. Louis T. Byars, 306 N. Grand Blvd., St. Louis.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: *Oral.* New York, December. Final date for filing application is Sept. 15. Sec., Dr. Francis J. Braceland, 162-110 Second Ave., S. W., Rochester, Minn.

AMERICAN BOARD OF RADIOLOGY: *Oral.* Boston, Nov. 26-30. Final date for filing application is Aug. 1. Sec., Dr. R. R. Kinkle, 162-110 Second Avenue, S. W., Rochester, Minn.

AMERICAN BOARD OF UROLOGY: Chicago, February. Final date for filing application is Nov. 1. Sec., Dr. Harry Culver, 1409 Wilder St., Minneapolis 4.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Governmental Hospital: Right of City Hospital to Remove Physician from Regular Staff.—The plaintiff filed suit to enjoin the defendant city from suspending him from the staff of a hospital which it operates. From an order denying an injunction, the plaintiff appealed to the Supreme Court of Florida.

Regulations governing the operation of the municipal hospital of Lakeland were approved by the city in 1943. Among other things, these regulations provided that "(A) The regular staff shall consist of those physicians, surgeons and dentists practicing in the city of Lakeland who have been, or may be, appointed by the Staff Executive Committee as hereinafter provided, and whose memberships have been approved by the City Commissioners." In relation to suspension of members of the staff, the regulations provided that "(19) Dismissal from Membership. Suspension. Members of the staff may be recommended for suspension or dismissal for unprofessional conduct or for the violation of the rules of the staff or of the hospital. Charges against staff members must be in writing to the president of the staff, who will refer the matter to the executive committee for investigation and recommendations, after which a vote of the staff shall be taken without discussion. A two thirds majority vote by secret ballot shall be necessary for the suspension or dismissal of the staff member. All staff members must be notified in writing of such contemplated action at least two weeks prior to the time of taking vote." The executive committee referred to in paragraph 19 consists of five members of the regular staff elected at the annual meeting each year. It serves for a period of one year, and to it is designated the duty to investigate any complaints that arise pertaining to the efficiency of the hospital or to irregularities of staff members. The plaintiff applied for membership on the regular staff in 1944, his application stating (in accordance with the approved form) "I agree to abide by the rules and regulations of the medical staff as approved by the city commission. I also agree to keep accurate and up to date records of patients under my care and complete their records within seventy-two hours after discharge of patient. I also agree to attend 75 per cent of the meetings of the staff." The permit issued to the plaintiff and approved by the city commission contained substantially the same provisions. On Nov. 1, 1945 the city manager issued the following directions: "To all staff members: Please be advised that beginning on the above date the supervisor of each floor has been instructed not to permit any patient to be taken to surgery unless the following is recorded on the patient's chart: 1. A complete physical examination. 2. Preoperative diagnosis. 3. Laboratory report. Also on all cases of therapeutic abortion there must be recorded two consultations with other physicians, one of which must be an obstetrician. This matter was brought up for discussion at a meeting of the executive committee of the medical staff held Oct. 31, 1945 and motions made, seconded and carried that the above ruling be enforced."

On Jan. 16, 1946 the superintendent of the hospital notified the plaintiff of a meeting of the executive committee on that day and urged the plaintiff to attend, which he did. The meeting was concerning the plaintiff and his noncompliance with the hospital regulations. The executive committee met again on February 12, and the plaintiff was invited to attend that meeting but he did not do so. On March 8 the committee held another meeting to which plaintiff was invited. He did not attend, stating that the committee could do as it pleased. On March 12 formal charges were given the plaintiff, and the executive committee granted him seventy-two hours in which to answer the charges and set March 15 as the day for further hearing. At the March 12 meeting, however, the committee made a formal report of charges but explained to the plaintiff that, although notice to the staff for a meeting on March 26 had been sent out, the executive committee would gladly hear any explanation which he wished to make. The plaintiff did not attend the meeting scheduled for March 15. On March 26, after the required two weeks notice, the staff voted to recommend to the city commissioners, and did recommend the next day, the indefinite suspension of the plaintiff from the staff for repeated unprofessional conduct. On April 4 the city commission met for the purpose of determining whether or not to suspend the plaintiff from the staff of the hospital. The plaintiff had been notified of this meeting and requested to attend. He was represented instead by his attorney, who read a letter which informed the city commission that the plaintiff had filed suit to secure such relief as it was possible for the court to allow under the law but asked for no action by the city commission. After the letter had been read, the attorneys were asked if they had any further statement to make. They had nothing more to say and left the meeting. The city commissioners then approved the recommendations of the staff and suspended the plaintiff.

The Supreme Court said that it was not incumbent on the city to maintain a hospital for the private practice of medicine and that a physician does not have a constitutional or statutory right to practice his profession in the city's hospital. It is well recognized, the court continued, that reasonable rules and regulations may be prescribed concerning the qualifications of physicians permitted to practice in public hospitals and follows that reasonable rules and regulations may also be imposed on physicians regulating their practice within the hospital. The management of the affairs of the city's hospital was in the exercise of a proprietary or corporate capacity as distinguished from one governmental in nature. Even though the hospital be a public hospital, plaintiff as a physician had no right (per se) to practice in the hospital, it being a privilege rather than a right. The court admitted that the city commission has no right to exercise its power in an unreasonable, arbitrary and capricious manner without being subject to judicial review but concluded that in the case presented such behavior was not made to appear. Accordingly the order of the trial court denying plaintiff's injunction was affirmed.—*Bryant v. City of Lakeland, 28 So. (2d) 106 (Fla., 1946).*

Medical Motion Pictures

FILM REVIEW

Manual Rotation in the Management of Occiput Posterior and Occiput Transverse Positions. Directed by H. J. Holloway, M.D., and E. S. Burge, M.D. Produced in 1943 by the Department of Obstetrics and Gynecology, Northwestern University Medical School and the Evanston Hospital. Photography by Mervin W. LaBuz. 16 mm., color, silent, 1,100 feet (one reel). Showing time thirty-two minutes. Procurable by rental, $4, or by sale from Audio-Visual Medical Education Department, Northwestern University Medical School, 303 East Chicago Avenue, Chicago 11.

This is a teaching film intended for medical students and others interested in obstetric problems. Position diagnosis, manual rotation of occiput to an anterior position, forceps application and extraction for each of the posterior and transverse positions are explained and clearly illustrated. These technics are demonstrated in detailed steps, first on a "manikin" and then on a patient during an actual delivery. Many other details incidental to delivery are well illustrated, including constant observation of fetal heart tones, correlation of physical findings elicited by vaginal or rectal and abdominal examination, bladder emptying immediately prior to delivery, making of an episiotomy, and inspection and repair of the cervix after delivery.

The authors stress three requirements for successful accomplishment of the maneuver described: (1) accurate diagnosis of position, station and dilatation, (2) good muscular relaxation (they use drop ether anesthesia) and (3) a competent obstetrician. The photography is excellent, while the printed titles do not seem to furnish adequate explanatory remarks, this may have been intentional so that each instructor using this film for a class of students might supply his own narrative.

The film is recommended for showing to students or others interested in obstetric problems. It displays clearly many basic obstetric principles as well as the special maneuver described by the authors.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1937 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied with stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

Alabama State Medical Assn. Journal, Montgomery

16:317-352 (April) 1947

Penetration Operation for Deafness. J. B. Farrior.—p. 317.
Acute and Subacute Yellow Atrophy of Liver: Report of 3 Cases with Necropsy. J. L. Chesnut.—p. 322.
Cystic and Caseous Tuberculosis of Multiple Bones: Case Report. C. W. C. Moore and L. L. Friedman.—p. 332.

16:353-404 (May) 1947

Menopause Syndrome. E. H. Sanders.—p. 353.
Medicine and National Security. E. H. Berta.—p. 357.
Neurosurgical Relief of Intractable Pain. W. G. Haynes and S. E. Graham.—p. 364.

American Heart Journal, St. Louis

33:413-556 (April) 1947

*Observations on Volume of Pulmonary Circulation and Its Importance in Production of Cyanosis and Polycythemia. H. B. Taussig and A. Blalock.—p. 413.
Studies on Coronary Circulation: Collateral Circulation of Normal Human Heart by Coronary Perfusion with Radioactive Erythrocytes and Glass Spheres. M. Prinzmetal, B. Simkin, H. C. Bergman and H. E. Kruger.—p. 420.
*Incidence of Thromboembolic Lesions Accompanying Myocardial Infarction. H. K. Hellerstein, and J. W. Martin.—p. 443.
Experimental Method for Closure of Interauricular Septal Defects in Dogs. R. Cohn.—p. 453.
Tolerance of Human Heart to Acidosis: Reversible Changes in RS-T Interval During Severe Acidosis Caused by Administration of Carbon Dioxide. M. D. Altschule and W. M. Waverly.—p. 458.
Influence of Heart Size on the Circulation Time. M. H. Nathanson and S. R. Elek.—p. 464.
Preliminary Study of Coronary Circulation Post Mortem. A. H. Salans and Phyllis Tweed.—p. 477.
*Further Observations on Treatment of the Anginal Syndrome with Thiouracil. S. Ben-Asher.—p. 490.
Raynaud's Disease in Men. D. I. Abramson and H. B. Shumacker Jr. —p. 500.
Traumatic Rupture of the Aorta. G. Strassmann.—p. 508.

Pulmonary Circulation in Cyanosis and Polycythemia.—Taussig and Blalock show that diminished blood flow to the lungs, such as occurs in the tetralogy of Fallot, causes unsaturation of the arterial blood. When this is extreme and persistent, the condition leads to the development of polycythemia. In patients in whom the cyanosis and polycythemia result from lack of adequate circulation to the lungs, increasing the circulation to the lungs increases the oxygen saturation of the arterial blood, lessens the cyanosis and leads to a reduction in the polycythemia. Oxygen saturation of 75 to 88 per cent can usually be attained in patients with a tetralogy of Fallot by an anastomosis of the proximal end of the innominate artery to the side of one of the pulmonary arteries. At such a level of oxygen saturation of the arterial blood the stimulus for the production of polycythemia has been withdrawn. An oxygen saturation of 65 to 70 per cent may be sufficient to enable the child to indulge in unrestricted activity and does not necessarily lead to the development of polycythemia.

Thromboembolic Lesions in Myocardial Infarction.—Hellerstein and Martin studied the incidence and severity of thromboembolic lesions following myocardial infarction in 160 cases of myocardial infarction encountered in 2,000 consecutive necropsies. Of the 160 cases of myocardial infarction 73 (45 per cent) presented a total of 111 thromboembolic lesions. Peripheral infarcts were a main or contributory cause of death in 43 of 160 cases. The use of anticoagulants is thought to be warranted when proper control is available.

Treatment of Anginal Syndrome with Thiouracil.—Ben-Asher found that thiouracil was beneficial to 25 of 37 patients with the anginal syndrome and that the smaller dose of 0.4 Gm. is almost as effective as the larger dose of 0.6 Gm. Toxic reactions may occur with both. Five patients developed fever in the first ten days of treatment. Three patients developed neutropenia in the fourth month of treatment.

American J. Digestive Diseases, Fort Wayne, Ind.

14:121-152 (April) 1947

*Nutritional Survey at a Children's Institution: Incidence of Avitaminotic Lesions and Effects of Therapy. M. S. Biskind and R. R. Williams. —p. 121.
An Instructive Case of Treated Hepatic Disease, with a Twenty-Seven Year Follow-Up. B. B. V. Lyon.—p. 130.
Diabetes Mellitus, Fibrocongestive Splenomegaly (Banti's Syndrome) and Infectious Mononucleosis. L. L. Peacock and L. E. Lieber.—p. 135.
A Soluble Phenolphthalein Laxative. M. Rosenthal, S. E. Cairncross and M. G. Gray.—p. 143.

Incidence of Avitaminotic Lesions in Children's Institution.—Biskind and Williams studied 183 institutionalized boys of the age group 8 to 17 for signs and symptoms of nutritional deficiency. The boys had been sent to the institution because of behavior problems. The institution was situated in the country on a large tract of land. There was an unexpectedly high incidence of signs and symptoms of nutritional deficiency. Approximately 90 per cent had glossitis, 67 per cent had gingivitis, 19 per cent had cheilosis and 60 per cent had avitaminotic symptoms related to the nervous system. Routine nutritional therapy with the vitamin B complex, together with ascorbic acid and vitamins A, D and E, of all but a few of this group during a period of seven months led to a complete disappearance of the signs of deficiency in most of those affected and improvement in all but a few of the residual group. This study supports the view that examination for and adequate treatment of the stigmas of nutritional deficiency should have high priority in routine medical care.

American Journal of Physiology, Baltimore

160:1-276 (April) 1947. Partial Index

Lipid Metabolism and Development of Anemia in Splenectomized Guinea Pigs Fed Cholesterol. Barbara Kennedy and Ruth Okey.—p. 1.
Modification of Respiratory Movements by Vagal Stimulation. H. V. Rice and Margaret S. Joy.—p. 24.
Respiratory and Circulatory Response of Normal Man to Inhalation of 7.6 and 10.6 per cent Carbon Dioxide with Comparison of Maximal Ventilation Produced by Severe Muscular Exercise, Inhalation of Carbon Dioxide and Maximal Voluntary Hyperventilation. R. D. Dripps and J. H. Comroe Jr.—p. 43.
Factors Affecting Electrical Potential of Gastric Mucosa. H. V. Rice and R. T. Ross.—p. 77.
Interaction of Prothrombin A and B. F. L. Munro and Muriel P. Munro.—p. 95.
Effect of Insulin on Food Intake After Vagotomy and Sympathectomy. M. I. Grossman, G. M. Cummins and A. C. Ivy.—p. 100.
Effect of Various Degrees of Anemic Anoxia on Water Distribution in Body. J. J. Lawless and E. J. Van Liere.—p. 103.
Influence of Test Meal Composition on Gastric Emptying in Man. A. Henschel, A. Keys, Angie Mae Sturgeon and H. L. Taylor.—p. 107.
Active Principle of Placental Toxin: Thromboplastin; Its Inactivator in Blood; Antithromboplastin. C. L. Schneider.—p. 123.
Renal Clearance of Essential Amino Acids Arginine, Histidine, Lysine and Methionine. L. D. Wright, H. F. Russo, Helen R. Skeggs, Elizabeth A. Patch and K. H. Beyer.—p. 130.
Further Observations on Factors Influencing the Biochemical Appraisal of Nutritional Status. G. H. Berryman and C. R. Henderson.—p. 142.
Studies on Frost Bite, with Special Reference to Treatment and Effect on Minute Blood Vessels. R. Quintanilla, F. H. Krusen and H. E. Essex.—p. 149.
Effect of Pilocarpine, Mecholyl, Atropine and Alcohol on Gastric Potential and Secretion of Hydrochloric Acid. W. S. Rehm and L. E. Hahn.—p. 162.
Effect of Heavy Muscular Work on Volume of Circulating Red Corpuscles in Man. G. Nylin.—p. 180.
Effect of Experimental Insomnia on Rate of Potential Changes in Brain. D. B. Tyler, J. Goodman and T. Rothman.—p. 185.
*Thermal Responses and Efficiency of Sweating when Men are Dressed in Arctic Clothing and Exposed to Extreme Cold. H. S. Belding, H. D. Russell, E. C. Darling and G. E. Folk.—p. 204.

Thermal Responses and Sweating in Extreme Cold.—Belding and his associates obtained data on sweating, moisture uptake of the clothing, energy expenditure, pulmonary ventilation, skin temperature, rectal temperature and comfort in men

who performed various activities while they were exposed to cold but were dressed in arctic uniform. The sweating of different subjects under identical conditions varied widely, between about 350 and 725 Gm. per hour. The subjects who sweated more generally had higher skin and rectal temperatures as well as higher pulse rates and greater energy production. At temperatures between 40 and —40 F. most of the sweat secreted was taken up by the clothing. When sweating was moderate the uptake was confined to the outer layers, but when profuse the underclothing was soaked. A hypothesis was formulated that the transfer of sweat from the skin depends (*a*) on the vapor pressure difference from layer to layer in the system consisting of skin, clothing layers and ambient air and (*b*) on the specific resistance to vapor transfer provided by the fabrics and the air trapped in the clothing. Because the vapor pressure difference between the relatively warm inner layers and the cool outer layers is large there is little tendency to pick up moisture unless sweating is profuse; however, the vapor pressure difference between the cool outer layers and the environment is small, with the result that much of the sweat secreted accumulates in the outer garments. Sweating was shown to be an inefficient way to achieve body cooling when men are heavily dressed in the cold because much of the sweat originally evaporated at the skin is recondensed in the clothing, giving back a portion of the heat of condensation to the skin. The data suggest that when it is possible for men to modify their activity to the point of feeling "cool but comfortable" during arctic exposures sweating and accumulation of moisture in the clothing will be minimal.

American Practitioner, Philadelphia

1:401-458 (April) 1947

Influence of Complications on the Treatment of Peptic Ulcer. L. D. Snorf.—p. 401.
Amino Acids in Nephrosis. D. A. MacFadyen.—p. 405.
Recognition of Acute Bacterial Endocarditis. H. H. Hussey Jr.—p. 409.
Short Term Psychotherapy. Harriet Hunter.—p. 412.
Edema in Chronic Nephritis: Its Mechanism and Management. R. Schwartz.—p. 419.
Rocky Mountain Spotted Fever. G. T. Harrell, J. K. Aikawa and W. M. Kelsey.—p. 425.
Differential Diagnosis and Symptomatic Treatment in the Asthmatic Patient. R. Chabot.—p. 436.

Archives of Internal Medicine, Chicago

79:365-474 (April) 1947

*Treatment of Plasmodium Vivax Malaria of Foreign Origin: Comparison of Various Drugs. H. H. Gordon, F. R. Dieuaide, A. Marble, H. B. Christiansen and L. K. Dahl.—p. 365.
Coexisting Tuberculosis and Coccidioidomycosis. H. Rifkin, D. J. Feldman, L. E. Hawes and L. E. Gordon.—p. 381.
Septic Staphylococcemia Successfully Treated by Penicillin and Bacteriophage. W. J. MacNeal, Anne Blevins and R. McGrath.—p. 391.
*Hemolytic Streptococcic Sore Throat: Poststreptococcic State. L. A. Rantz, P. J. Boisvert and W. W. Spink.—p. 401.
Cardiac Failure in Penicillin Treated Subacute Bacterial Endocarditis. M. J. Fiese.—p. 436.
*Mercurial Diuretics: Comparison of Acute Cardiac Toxicity in Animals and Effect of Ascorbic Acid on Detoxification in Their Intravenous Administration. D. W. Chapman and C. F. Shaffer.—p. 449.
Experimentally Induced Infectious Hepatitis: Roentgenographic and Gastroscopic Observations. W. P. Havens Jr., S. D. Kushlan and M. R. Green.—p. 457.
Epileptogenic Effects of Penicillin: Experimental Study. C. Pilcher, W. F. Meacham and E. R. Smith.—p. 465.

Various Drugs in Treatment of Plasmodium Vivax Malaria.—Gordon and his associates describe the immediate response to therapy and minor toxic symptoms after the use of various drugs and on the rates of relapse following administration of quinacrine hydrochloride, SN 6911 and chloroquine. Neither SN 6911 nor chloroquine was more effective than quinacrine hydrochloride in curing patients of relapses. Some evidence was collected that SN 8137 would be ineffective. The interval until relapse in a small number of patients was shorter following use of SN 6911 than following use of chloroquine or quinacrine hydrochloride. All three drugs were found to be effective in controlling the parasitemia and fever of the relapse and to cause the patient relatively few minor toxic symptoms. Because none of them stain the skin and because the widespread use of quinacrine hydrochloride has led to the development of sensitivity to the drug in a small percentage of soldiers, the drugs tested may prove of value as a substitute for quinacrine hydrochloride in therapy of the acute attack. All four synthetic drugs were superior to quinine sulfate.

The Poststreptococcic State.—Rantz and his associates studied a large number of cases of sore throat caused by group A hemolytic streptococci in military personnel. Convalescence in many instances was marred by a complication. Often this was the result of local suppuration, but in approximately 20 per cent of all cases a disorder supervened which could not be demonstrated to be the result of the local extension of the initial process in the throat or the invasion of remote tissues by hemolytic streptococci. Arthritis was the commonest type of late nonsuppurative complication. Involvement of the joints was associated in certain cases with fever and clinical and/or electrocardiographic evidence indicating the presence of carditis. Such cases were then indistinguishable from cases of classic rheumatic fever. The convalescence of another group of patients was complicated by a recrudescence of fever after a period of normal temperature following the initial respiratory illness. Evidence of carditis in the form of abnormal electrocardiograms was discovered in more than one third of these cases. This febrile disease, except for the absence of involvement of the joints, closely resembled the arthritic poststreptococcic disorder. The treatment of the acute phase of hemolytic streptococcic sore throat by large amounts of sodium salicylate, a short course of penicillin alone or followed by a sulfonamide compound or the use of the latter drug alone did not prevent late nonsuppurative complications. Poststreptococcic disorders were not observed in a small group of men who received 500,000 to 1,000,000 units of penicillin in eighty hours, but these results are not convincing, since the number of patients so treated was small.

Ascorbic Acid in Detoxification of Mercurial Diuretics Given Intravenously.—Chapman and Shaffer extended the investigation of the mechanism of immediate death in dogs from mercurial diuretics for the three commonly employed ones, mercurophylline injection, mersalyl and theophylline and mercuhydrin. They also studied the possible detoxifying effect of ascorbic acid on these preparations. Their experiment proved that mercuhydrin was the least toxic of the three mercurial diuretics studied. The administration of ascorbic acid prior, to or simultaneously with mercuhydrin reduced the toxicity of this preparation, but when given with mercurophylline injection and with mersalyl and theophylline it had no detoxifying effect. The usual mechanism of death produced by mercuhydrin, with and without ascorbic acid, was ventricular asystole and by mercurophylline injection and mersalyl and theophylline was ventricular fibrillation. Twenty patients with cardiac failure who have received mercuhydrin with ascorbic acid intravenously to date have had an equal or an increased diuresis up to 50 per cent.

Archives of Ophthalmology, Chicago

37:403-560 (April) 1947

Disease Processes versus Disease Pictures in Interpretation of Retinal Vascular Lesions. J. S. Friedenwald.—p. 403.
Aims and Aids in Teaching of Basic Sciences in Ophthalmology. D. G. Cogan.—p. 428.
Primary Lipid Dystrophy of the Cornea. A. Davidson.—p. 433.
Esotropia Following Occlusion. K. C. Swan.—p. 444.
Pentothal Sodium in Ophthalmic Surgery. G. J. Thomas and M. F. McCaslin.—p. 452.
Optokinetic and Other Factors Modifying Vestibular Nystagmus. J. W. Henderson.—p. 459.
Changes in Retinal Arterioles Associated with Hypertensions of Pregnancy. A. V. Hallum.—p. 472.
*Ophthalmoscopic Changes Associated with Hypertensive Vascular Disease as a Guide to Sympathectomy. M. Cohen.—p. 491.
Keratoconjunctivitis Due to Diphtheroid-like Organism: Report of Case. R. R. Chace and D. Locatcher-Khorazo.—p. 497.
Sensorial Retinal Relationship in Concomitant Strabismus. H. M. Burian.—p. 504.

Fundus Changes in Hypertensive Vascular Disease as Guide to Sympathectomy.—Cohen examined the fundi of 90 patients with essential hypertension who were to undergo surgical intervention. The fundi were examined frequently before and after operation. Each patient was required to remain one or

two weeks in the hospital prior to the thoracolumbar sympathectomy in order that the effects of rest and of the sodium amytal test on the diastolic pressure might be studied. No progression of retinal lesions was observed after sympathectomy in 82 patients with benign essential hypertension. Regression of the retinal hemorrhages, exudates and edema were observed after sympathectomy in 22 of 60 patients in whom hypertension was associated with moderate fundic lesions, but the arteriolar sclerosis remained unchanged in 48. Retinal angiospasm was relieved in 12 patients. Cases of benign essential hypertension showing normal eyegrounds or mild or moderate fundic lesions are suitable for sympathectomy if continued medical treatment is of no avail in alleviating the severe and persisting subjective symptoms. The group of patients who had so-called malignant (rapidly progressive) hypertension with extensive fundic lesions was too small to lead to any conclusion. The chief purpose of sympathectomy is the relief of subjective symptoms in patients with essential hypertension.

California Medicine, San Francisco

66:213-276 (April) 1947

Public Relations of a State Medical Society. J. W. Cline.—p. 213.
*Some Clinical Aspects of Rheumatic Fever in the Adult on the Pacific Coast. M. Eliaser Jr.—p. 217.
The Electrocardiogram in Diagnosis and Management of Rheumatic Fever.—p. 221.
*Differential Diagnosis of Adult Rheumatic Fever and Rheumatoid Arthritis. E. P. Engleman.—p. 227.
Public Measures for the Control of Rheumatic Fever in England. J. Parkinson.—p. 230.
Rheumatic Fever Control Program in California. H. Rosenblum.—p. 233.
Diagnosis and Treatment of Arteriovenous Aneurysm in a Naval Hospital. G. A. Stevens.—p. 235.
Fractional Spinal Anesthesia for Short Upper Abdominal Surgery. J. Brill and D. E. Stewart.—p. 238.
Poison Oak: New Antigens and Effect on Sensitized Patients. E. K. Stratton.—p. 240.
Newer Drugs for Allergic Disorders and Their Place in the Histamine Theory. M. M. Hartman.—p. 242.
Progress in Treatment of Carcinoma of the Prostate. A. J. Scholl.—p. 249.

Clinical Aspects of Rheumatic Fever in Adults.—Eliaser observed that hemolytic streptococcic infections, including scarlet fever, are common precursors of the acute disease in the adult and are followed by a two to three week period during which extremely strenuous physical activities do not produce symptoms. Clinically significant cardiac murmurs were audible in 45 per cent of the patients at the onset of the disease. Probable valvulitis was revealed in 15 per cent at the onset but was not detectable following convalescence. The involvement of joints among adult patients developing their initial attack in the Pacific Coast area is relatively mild compared to that described in children in several other parts of the United States. The duration of the active phase of the disease averaged sixty-three days.

Adult Rheumatic Fever and Rheumatoid Arthritis.—Engleman says that experience during the last war has stressed the difficulty of differentiating between adult rheumatic fever and rheumatoid arthritis. A comparative study was made of 252 soldiers with active rheumatic fever with carditis and 33 soldiers with acute, "atypical" rheumatoid arthritis. Carditis, when present, usually indicates rheumatic fever, although not necessarily so. The arthritis of atypical rheumatoid disease is apt to be progressive and not migratory, while in adult rheumatic fever it may be either progressive or migratory. The progression of the arthritis may be slower in rheumatoid disease than in rheumatic fever. Unlike rheumatic fever, the antecedent upper respiratory infection is infrequent in rheumatoid arthritis, and when it does occur the latent period is usually shorter. The ineffectiveness of salicylates characterizes rheumatoid arthritis. In rheumatic fever the objective joint improvement is dramatic with the proper administration of salicylates. Erythema, purpura and signs of pulmonary or pleural involvement should favor the diagnosis of rheumatic fever. The elevated sedimentation rate of rheumatoid arthritis continues for a prolonged period, while in most cases of rheumatic fever it is of comparatively short duration.

Canadian Journal of Public Health, Toronto

37:111-156 (March) 1947

Some Observations on the Prevalence of Rheumatic Heart Disease in Canada. J. D. Keith and L. A. Pequegnat.—p. 111.
Clinical Study of Neurotic Disorders in the Plant. J. A. Walters.—p. 118.
*Plague, Rocky Mountain Spotted Fever and Tularemia Surveys in Canada. F. A. Humphreys and A. G. Campbell.—p. 124.
Study of Diphtheria Antitoxin Response to Recall Doses of Specific Antigen. F. O. Wishart and Marie Rose Reid.—p. 131.
Standardization of Influenza Vaccine by Red Cell Agglutination and Antigenic Tests in Mice. R. Hare and Dorothy M. Mackenzie.—p. 141.

Plague, Rocky Mountain Spotted Fever and Tularemia in Canada.—Humphreys and Campbell present the results of an eight year survey on the plague, Rocky Mountain spotted fever, and tularemia in western Canada. Plague infection (Pasteurella pestis) is prevalent in ground squirrels in a large area of southeastern Alberta and in the adjoining territory of Saskatchewan. Six of 817 tissue pools and 32 of 939 flea pools submitted from 12,676 ground squirrels collected in Alberta, and 2 of 356 flea pools obtained from 7,448 ground squirrels in Saskatchewan proved positive. The infectious agent of Rocky Mountain spotted fever (Rickettsia dermacentroxenus) occurs in ticks in both British Columbia and Alberta. Evidence of the infection was found in 5 specimens out of a total of 72,227 ticks collected in British Columbia and in 10 out of 49,201 collected in Alberta. Pasteurella tularensis was encountered a total of thirty-eight times in the examination of specimens—ground squirrels, rabbits, mice, certain birds and ticks—submitted from various localities for evidence of plague and Rocky Mountain spotted fever.

Cincinnati Journal of Medicine

28:233-300 (April) 1947

Ambulatory Diabetic and the Family Doctor. E. P. Joslin.—p. 233.
*Lymphadenopathy in Association with Thiouracil Therapy. M. B. Macht and J. A. Herschfus.—p. 243.

Lymphadenopathy in Thiouracil Therapy.—Macht and Herschfus state that a survey of approximately 7,000 cases of thyrotoxicosis in which thiouracil has been employed indicates that toxic reactions occur in about 14 per cent. Lymphadenopathy as a complication was observed in relatively few cases. In a woman aged 67 lymphadenopathy had a dramatic onset eleven weeks after the treatment with thiouracil had begun. The lymph node enlargement was greater than any heretofore reported. The absence of any abnormal lymphocytes in the blood smears and the normal heterophile agglutination precluded the diagnosis of infectious mononucleosis. A malignant lymphoma was ruled out by the rapid progression of the nodes and the inflammatory nature of the reaction. Oral sepsis in the absence of agranulocytosis has been reported as a complication of thiouracil therapy, and this patient's buccal ulcers may have been caused in the same manner. The subsidence of the lymphadenopathy on withdrawal of thiouracil and the lack of other known etiologic factors suggest that the enlargement was a direct result of thiouracil.

Connecticut State Medical Journal, Hartford

11:161-234 (March) 1947

Diagnosis of Peripheral Arterial Diseases. H. Montgomery.—p. 168.
Tumor Clinics of Connecticut. E. J. Ottenheimer.—p. 167.
Progress in Treatment of Alcoholism. R. Reynolds.—p. 170.
Medical Program at Newington Veterans Hospital. L. G. Beardsley.—p. 173.
Rooming-In Plan for Mothers and Newborn Infants. Edith B. Jackson and H. Thomas.—p. 175.
Waterbury Hospital Clinical Pathologic Conference. J. O. Collins.—p. 177.
Psychosomatic Elements—When Foreman Is Pain in Neck. C. C. Burlingame.—p. 179.

11:235-318 (April) 1947

Operation of Public Law 725: Hospital Survey and Construction Act. H. E. Hilleboe.—p. 242.
Modern Influences in Medical Practice. T. P. Murdoch.—p. 245.
Present Status of Streptomycin in Treatment of Tuberculosis. H. C. Hinshaw, W. H. Feldman and Marjorie Pyle.—p. 247.
Common Anal and Rectal Problems. J. G. Buie.—p. 250.
Clinical Use of Fluoroscein. H. M. Kaplan and L. F. Hastings.—p. 254.
Soft Tissue Sarcoma—Ten Year Survival Following Roentgen Ray Therapy. H. M. Nachman and P. D. Rossbach.—p. 257.
Voluntary Medical Prepayment Plans as They Apply to Rural Communities. J. R. McVay.—p. 265.

Endocrinology, Springfield, Ill.

40:123-230 (March) 1947

Pigmentation and Hair Growth in Black Rats as Modified by Chronic Administration of Thiourea, Phenyl Thiourea and Alpha-Naphthyl Thiourea. S. H. Dicke.—p. 123.
Differentiation of Antithyroid Action of Thiouracil, Thiourea and Para-Aminobenzoic Acid from Sulfonamides by Iodide Administration. C. G. Mackenzie.—p. 137.
Effect of Vagotomy and Thoracic Sympathectomy on Blood Glucose Changes in Dogs Given Alloxan. E. G. Shipley and K. H. Beyer. —p. 154.
Inhibition of Thyroid Function in Beagle Puppies by Propylthiouracil Without Disturbance of Growth or Health. E. Mayer.—p. 165.
Relation of Hypophysis, Ovary, Placenta and Fetus to Development of Anemia During Last Half of Pregnancy in Rat. J. S. Newcomer. —p. 182.
Estrogenic Activity of Rabbit Whole Blood Determined by the Intravaginal Pellet Method. B. Krichesky.—p. 192.
Effect of Prostate and Seminal Vesicle on Production of Hyaluronidase by Rat Testes Homogenate. S. L. Leonard, P. L. Perlman and R. Kurrasch.—p. 199.
Effect of Gonadectomy and Administration of Testosterone Propionate on Growth of Antlers in Male and Female Deer. G. B. Wislocki, J. C. Aub and C. M. Waldo.—p. 202.

Georgia Medical Association Journal, Atlanta

38:105-154 (March) 1947

Peptic Ulcer: Review of Present Day Treatment. R. F. Norton.—p. 105.
Thiouracil in Treatment of Toxic Goiter, and Its Dangers. T. C. Davison and A. H. Letton.—p. 112.
Surgery on Elderly Patients. W. W. Baxley.—p. 116.
Subphrenic Abscess. J. W. Turner.—p. 119.
One Year's Operation of Expanded Typhus Control Program in Georgia. R. J. Boston.—p. 124.

38:155-184 (April) 1947

Topical Application of Thrombin and Plasma in Split Skin Grafts. C. E. Rushin.—p. 355.
Present Status of Pilonidal Cysts. M. C. Pruitt.—p. 153.
Importance of Early Diagnosis of Bladder Tumors. H. P. McDonald and A. J. Filip.—p. 162.
Spinal Anesthesia. J. M. Kellum.—p. 165.
Further Consideration of Malignant Lymphoma. J. Funke.—p. 168.
Surgery of Colon in Wartime: Experiences in Management of Reconstruction of Colon in Z. I. Hospitals. D. H. Poer.—p. 171.

Geriatrics, Minneapolis

2:75-136 (March-April) 1947

Precursors of Gastric Carcinoma. R. Schindler.—p. 75.
Anesthesia in the Aged. E. H. Watts.—p. 88.
Effect of Age on Leukocyte Count: Comparison of White Blood Cell Counts in Aged and Young Individuals, with Special Reference to Response to Infection. W. R. Gabbert, Lucile W. Hutaff and G. T. Harrell.—p. 96.
*Nutritional Aspects of Aging. H. A. Rafsky and B. Newman.—p. 101.
Cutaneous Hypersensitivity Reactions to Penicillin in the Aged. J. Farrington.—p. 105.
*Physical Fitness and Work Capacity of Older Men. E. Simonson. —p. 110.

Nutritional Aspects of Aging.—Rafsky and Newman say that there is evidence that in apparently normal aged persons there is a tendency to low blood levels and excretions of thiamine, low blood levels and high tolerance to ascorbic acid, a high incidence of porphyrinuria which disappears on the oral administration of nicotinic acid, and subnormal levels of carotene and vitamin A. Suggested as factors in explanation for these vitamin deficiencies have been inadequate intake of food, lack of vitamins in the diet, insufficient absorption of vitamins by the intestinal tract and failure of the organism to store vitamins. The authors describe investigations of these factors and stress that vitamin requirements of normal elderly people cannot be measured in terms of standards applicable to young adults or children. The diets of old people must be supplemented by vitamin therapy. Comparatively large amounts of vitamin supplement should be prescribed. Clinical experience has shown that at times it is essential to give these vitamins parenterally at the outset and then follow with vitamin therapy by mouth.

Physical Fitness and Work Capacity of Older Men.—Simonson thinks that if employment of older people does not more or less parallel the age shift, serious socioeconomic consequences will result. This raises the question whether increase of life expectancy is associated with a better maintenance of working capacity. If it is, an extension of the period of employment is feasible without important change in work. If, however, extension of the life expectancy is not paralleled by a similar age extension of working capacity, industrial jobs must be adapted to the working capacity of older men in order to maintain their employment. The second important question is whether the various physiologic, biochemical and psychologic functions deteriorate with age at the same rate. The third fundamental problem concerns the possibility of counteracting or delaying the decrease in working capacity with age. The author reviews the information available on these three fundamental problems and shows that much additional information is needed.

Journal of Aviation Medicine, St. Paul

18:109-216 (April) 1947

Rate of Nitrogen Elimination from Body Through Lungs. C. D. Stevens, H. W. Ryder, E. B. Ferris and M. Inatome.—p. 111.
*Electronic Warning Device for Oxygen Breathing Systems. C. A. Tobias and W. Siri.—p. 133.
Studies on Positive Pressure Respiration: Effect of Continuous Pressure Breathing on Arterial Blood Gases at High Altitude. A. L. Baruch, M. Eckman, I. Eckman and others.—p. 139.
Arterial Oxygen Saturation at Altitude. Margaret Henson, D. E. Goldman, H. R. Catchpole and others.—p. 149.
Influence of Cold On Efficiency of Man. S. M. Horvath and A. Freedman.—p. 158.
Occurrence of Bends, Scotomata and Hemianopsia at Altitudes Below 20,000 Feet. C. S. Houston.—p. 165.
Evaluation of Certain Tests of Physical Fitness. H. M. Pitt.—p. 169.
The Martinet. H. Porter.—p. 176.
Air Evacuation Activities. D. N. W. Grant.—p. 177.
Physical Principles Involved in Pilot Comfort and Efficiency. F. E. Randall and D. I. Pitt.—p. 184.
Medical Care of Casualties in Long Distance Air Evacuation. Grace H. Stakeman.—p. 192.
Changes in Pressure in Peritoneal Cavity Produced by Sudden Deceleration of Experimental Animals. R. F. Rushmer.—p. 199.

Electronic Warning Device for Oxygen Breathing Systems.—Tobias and Siri describe an electronic warning system for use in aircraft equipped with oxygen demand or pressure breathing systems. The device functions on the respiratory rate and is designed to indicate at a central warning panel any interruption in the respiratory cycle greater than fifteen seconds for all oxygen stations. The principle of operation is a time delay circuit which actuates the warning lights on the indicator panel. Operation of the system has proved satisfactory in both laboratory and flight tests.

Journal of Clinical Investigation, Boston

26:145-353 (March) 1947. Partial Index

Residual Effects of Phosgene Poisoning in Human Subjects. M. Galdston, J. A. Loetscher Jr., W. T. Longcope and N. L. Ballich.—p. 145.
Factors Influencing Urinary Excretion of Calcium: I. Normal Persons. Elizabeth L. Knapp.—p. 182.
Differential Spinal Block: Reactions of Sudomotor and Vasomotor Fibers. S. J. Sarnoff and Julia G. Arrowood.—p. 203.
Serum Potassium, Magnesium and Calcium Levels in Diabetic Acidosis. Helen E. Martin and Maxine Wertman.—p. 217.
Studies on Gangrene Following Cold Injury. F. A. Fahrman and J. M. Crimson.—p. 229.
Effect of Creatine on Pain of Muscle Ischemia. F. B. Culp and F. W. Kinard.—p. 277.
Scleroma: Etiologic Study. M. Gjelhaug Levine, R. E. Hoyt and J. E. Peterson.—p. 281.
Studies on Virus from Patient with Fort Bragg Fever (Pretibial Fever). H. Tatlock.—p. 287.
Electrophoretic Changes in Serum Protein Pattern of a Patient with Typhus Fever. V. P. Dole, A. Yeomans and N. A. Tierney.—p. 298.
Observations on Men Performing a Standard Amount of Work in Low Ambient Temperatures. S. M. Horvath and H. Golden.—p. 311.
Circulatory Dynamics in Basal State Observed During Convalescence: Changes in Body Weight, Blood Volume and Venous Pressure. G. R. Meneely, A. Segaloff and E. B. Wells.—p. 330.
*Sulfadiazine Resistant Streptococcal Infections in a Civilian Community. R. D. Johnson and T. L. Hartman.—p. 325.
Studies on Relationship of Hepatitis Virus to Persistent Symptoms, Disability and Hepatic Disturbance ("Chronic Hepatitis Syndrome") Following Acute Infectious Hepatitis. J. R. Neefe, J. Stokes Jr., R. S. Garber and S. S. Gellis.—p. 329.
Blood Lactate Response During Moderate Exercise in Neurocirculatory Asthenia, Anxiety Neurosis or Effort Syndrome. M. E. Cohen, F. Consolazio and R. E. Johnson.—p. 339.
Water Storage and Movements of Body Fluids and Chlorides During Acute Liver Disease. D. H. Labby and C. L. Hoagland.—p. 343.

Sulfadiazine Resistant Streptococcic Infections.—Johnson and Hartman point out that during a program of mass chemoprophylaxis of streptococcic infections in the armed forces it was observed that the effectiveness of such a regimen was

lost with the appearance of sulfonamide resistant strains of hemolytic streptococci. While these resistant strains spread in the U. S. Army and Navy, there had been no reports about epidemics in the civilian population due to sulfonamide resistant strains. Early in 1946 a small epidemic of scarlet fever occurred in Cooperstown, N. Y. Since the first 8 patients with scarlet fever were found to harbor type 19 hemolytic streptococci in their nasopharynxes, it was decided to determine whether they were sulfonamide resistant strains. All eight strains of hemolytic streptococci were found to be resistant to the action of sodium sulfadiazine in a concentration of 25 mg. per hundred cubic centimeters. From Feb. 15 to May 1, 1946 streptococcic infections were moderately prevalent in Cooperstown. A table lists the type distribution and sulfadiazine resistance of group A hemolytic streptococci obtained from 100 patients with scarlet fever, pharyngitis, otitis media, wound infections, blood stream infections and pneumonia. The most common streptococcus was type 3, which was responsible for 28 cases of hemolytic streptococcic infections. Type 19 was the cause of 24 cases of disease, with 23 of these strains being resistant to sodium sulfadiazine. None of these cases presented special therapeutic problems, nor were they clinically different from infections due to other types of hemolytic streptococci. The appearance of increasing numbers of bacteria which are resistant to various chemotherapeutic agents formerly effective against them suggests the desirability of a careful bacteriologic diagnosis of infectious agents prior to treatment with specific antibacterial drugs.

Journal of Infectious Diseases, Chicago

80:121-222 (March-April) 1947

Studies on Infection with Bacillus Anthracis: V. Isolation of Inflammatory Factor from Crude Extracts of Lesions of B. Anthracis Infection and Its Biologic and Chemical Relationship to Glutamyl Polypeptide. D. W. Watson, W. J. Cromartie, L. L. Bloom, R. J. Heckly, W. J. McGhee and N. Weissman.—p. 121.
Id.: VI. Physiologic Changes in Experimental Animals During the Course of Infection with B. Anthracis. W. L. Bloom, W. J. McGhee, W. J. Cromartie and D. W. Watson.—p. 137.
Id.: VII. Comparison of the Antibacterial Effects of Calf Thymus Histone and a Quarternary Ammonium Cationic Detergent on B. Anthracis. N. Weissman and L. H. Graf.—p. 145.
Reticuloendothelial Immune Serum (Reis): An Experimental Anemia in Bartonella Infected Rats Produced by Anti-Blood Immune Serum. C. M. Pomerat, E. H. Frieden and E. Yeager.—p. 154.
Studies on Hemoflagellates: I. A Semisolid Medium and Fluid Medium with Solid Base for Growing Various Species of Leishmania and Trypanosoma Cruzi. Shih Lu Chang.—p. 164.
Id.: Study of Growth Rates of Leishmania Donovani, L. Braziliensis, L. Tropica and Trypanosoma Cruzi in Culture. Shih Lu Chang and W. O. Nagler.—p. 172.
Occurrence in Human Serum of Inhibitory Substance to Hyaluronidase Produced by Strain of Hemolytic Streptococcus. G. J. Friou and H. A. Wenner.—p. 185.
Evaluation of Germicidal Agents by an Infection Prevention-Toxicity Method. E. H. Spaulding and A. Bondi Jr.—p. 194.
Inactivation of Murine Poliomyelitis Viruses by Heat. R. B. Lawson and J. L. Melnick.—p. 201.
Morphology of Cryptozoites and Metacryptozoites of Plasmodium Relictum and Relationship of These Stages to Parasitemia in Canaries and Pigeons. F. Coulston and C. G. Huff.—p. 209.
Skin Tests in Schistosomiasis Mansoni with Antigen from Heterologous Worms (Pneumoneces; Planaria). J. T. Culbertson, H. M. Rose and J. Oliver-Gonzalez.—p. 218.

Journal of Nervous and Mental Disease, New York

106:343-448 (April) 1947

Effect of Oral Administration of Lactic Acid on Clinical Course of Depressive States. H. Lowenbach and M. H. Greenhill.—p. 343.
The Gerstmann Syndrome: Case Report and Review of Literature. D. I. Arbuse.—p. 359.
Conditioned Psychogalvanic Response in States of Pathologic Anxiety. L. Welch and J. Kubis.—p. 372.
Experiences with Insulin and Electroshock Treatment in Army General Hospital. S. Paster and S. C. Holtzman.—p. 382.
Psychiatric Ward Management of the Acute Schizophrenic Patient. K. R. Eissler.—p. 397.
Epidemic of Encephalitis in Concentration Camp Terezin During the Winter 1943-1944. A. Kral.—p. 403.
Self-Induced Mediastinal Emphysema in a Psychotic: Attempt to Commit Suicide by Means of the Valsalva Experiment. M. P. Rosenblum and J. J. Silverman.—p. 414.
Report on 2 Cases of Psychosis with Oedipus Panic Treated Successfully with Electric Shock. P. S. Kraus.—p. 420.

J. Neuropathology and Exper. Neurology, Baltimore

6:111-216 (April) 1947

Deposition of Iron in Paraventricular Areas of Human Brain in Hemochromatosis. J. Cammermeyer.—p. 111.
Neuroglingenic Tumor of Diencephalon with Unusual Characteristics: Report of Case with Discussion of Classification. D. E. Fletcher and W. H. Bailey.—p. 128.
Neoplastic Transformation of Subependymal Cell Plate in Floor of Fourth Ventricle (Subependymal Spongioblastoma) with Clinicopathologic Case Report. H. Kuhlenbeck.—p. 139.
Parenchymatous Cortical Cerebellar Atrophy Associated with Pick's Disease. A. R. Buchanan, L. C. Overholt and K. T. Neuburger.—p. 152.
Relation of Spinal Subarachnoid and Perineurial Spaces. H. Somberg.—p. 166.
Cerebrospinal Fluid Pathways: Critical Note. G. B. Hassin.—p. 172.
Mechanism and Localization of Symptoms of Electroshock and Electronarcosis. A. van Harreveld.—p. 177.
Temporal Lobotomy. S. Obrador.—p. 185.
Extirpation of Cortical Arm Area as Defined by Stimulation Under Conditions of Primary Facilitation (Macaca Mulatta). J. P. Murphy and R. Arana.—p. 194.
Convulsant Effects of Penicillin on Cerebral Cortex. W. J. Burkowski and F. M. Forster.—p. 201.

Journal of Neurosurgery, Springfield, Ill.

4:97-190 (March) 1947

Further Uses of Gelatin Foam in Neurosurgery. E. F. Fincher.—p. 97.
*Resection of Greater Superficial Petrosal Nerve in Treatment of Unilateral Headache. W. J. Gardner, A. Stowell and R. Dutlinger.—p. 105.
*Dermatome Hypalgesia with Posterolateral Herniation of Lower Cervical Intervertebral Disk. J. J. Keegan.—p. 115.
Evidence of Active Invasion of Denervated Areas by Sensory Fibers from Neighboring Nerves in Man. W. K. Livingston.—p. 140.
Peripheral Nerve Injuries: II. Basic Data from Peripheral Nerve Registry Concerning 7,050 Nerve Sutures and 67 Nerve Grafts. B. Woodhall.—p. 146.
Experimental Hydrocephalus. F. D. Ingraham, E. Alexander Jr. and D. D. Matson.—p. 164.

Resection of Greater Superficial Petrosal Nerve in Unilateral Headache.—Gardner and his associates present evidence which indicates that periodic discharges of parasympathetic impulses over the greater superficial petrosal branch of the seventh nerve cause unilateral lacrimation, unilateral swelling and secretion of the nasal mucosa and unilateral head pain. Since these were the predominating symptoms in 3 cases observed by the authors within a short time, a diagnosis of "greater superficial petrosal neuralgia" appeared justified. In 1 of the 3 patients interruption of the nerve was resorted to in order to relieve the attacks. After listing seven methods by which attempts have been made to relieve neuralgias of the head, the authors say that in reviewing their own cases they found that since 1938 the greater superficial petrosal nerve has been divided 31 times in 26 patients for the relief of unilateral head pain. Most of these patients were benefited, some were not. The complications of the operation such as temporary facial paralysis and keratitis are discussed. The authors conclude that the operation provides a useful tool in the study and treatment of headache.

Dermatome Hypalgesia with Herniation of Cervical Disk.—Keegan says that the clinical syndrome of nerve root compression by posterolateral herniation of a lower cervical intervertebral disk has been well presented in recent articles by a number of observers. They have demonstrated that pain which extends from the lower cervical spine over the scapula and down the arm, often with associated numb sensation in some part of the hand, commonly is caused by lower cervical disk herniation. In the past this syndrome has been variously diagnosed as brachial neuritis, radiculitis, fibrositis, myalgia or reflex pain, with focal infection, cervical arthritis, acromial bursitis, cervical rib, scalenus anticus, cardiac or gallbladder disease often suspected in the etiology. Now it is necessary to reevaluate this type of pain and recognize that it more often is due to nerve root compression by herniation of a lower cervical intervertebral disk. Keegan stresses that the clinical syndrome of lower cervical disk herniation should be recognized as a fairly common cause of pain extending from the lower part of the neck over the scapula and down the arm with numbness of one or more digits of the hand. Unilateral herniation of a cervical disk compresses only one nerve root and gives rise to detectable sensory and motor loss in the distribution of that

root. Reduction of pain sensation or hypalgesia from single nerve root loss can be demonstrated by the technic of light pin scratch. Dermatome hypalgesia has been found in 51 clinical cases with history indicative of compression of a lower cervical nerve root by herniation of an intervertebral disk, presenting a new primary dermatome pattern for each of the fourth, fifth, sixth, seventh and eighth cervical nerve roots. Eight clinical cases of cervical rib or scalenus anticus muscle compression of the lower primary cord of the brachial plexus are presented to illustrate the distribution of the anterior primary division of the first thoracic and eighth cervical nerve roots, thus presenting a new diagnostic finding for this syndrome. A distinguishing symptom of lower cervical nerve root compression by herniation of an intervertebral disk is pain over the upper medial scapular region associated with neck movement. The presence of subjective and objective numbness or hypalgesia in an extremity is evidence of an organic lesion of a nerve to the extremity and cannot be classified as reflex pain. Nerve roots, determined by dermatome hypalgesia distributions, maintain a constant position; their location in relation to herniation of an intervertebral disk is more reliable than pathologic change in disks shown by x-ray examination or spinograms. A new dermatome chart of the human body is presented.

Journal of Nutrition, Philadelphia

33:361-490 (April) 1947

Some Effects of Methionine on the Utilization of Nitrogen in the Adult Dog. J. B. Allison, J. A. Anderson and R. D. Seeley.—p. 361.
Effect of Methionine on Urinary Nitrogen in Men at Normal and Low Levels of Protein Intake. R. M. Johnson, H. J. Deuel Jr., Margaret G. Morehouse and J. W. Mehl.—p. 371.
Amino Acids in Nitrogen Metabolism, with Particular Reference to Role of Methionine. Miriam Brush, Wanda Willman and Pearl P. Swanson. —p. 389.
Cevitamin Studies: VI. Effect of Tocopherol Supplementation on Output of Vitamin A, Carotene and Fat by Dairy Cows. P. L. Harris, W. J. Swanson and K. C. D. Hickman.—p. 411.
Observations on Nutritional Value of Dialyzed Whey Solids. F. K. Daniel and E. H. Harvey.—p. 429.
Nitrogen Retention Studies on Rats, Dogs and Man: Effect of Adding Methionine to an Enzymic Casein Hydrolysate. W. M. Cox Jr., A. J. Mueller, R. Elman and others.—p. 437.
Conjoint Effects of Varied Intakes of Thiamine and Vitamin A on Rats. Marie Dye, Thelma Porter and Eunice Kelly.—p. 459.
*Value of Meat and Peas, Alone or in Combination, as Source of Protein for Growth. W. P. Lehrer Jr., Ella Woods and W. M. Beeson. —p. 469.
Tissue Reserves of Ascorbic Acid in Normal Adults on Three Levels of Intake. J. Estelle Haines, Ann M. Klosterman, Hazel M. Hauck and others.—p. 479.

Meat and Peas as Source of Protein for Growth.—Lehrer and his associates point out that in low cost diets or when meats are difficult to obtain a common dietary recommendation is an increased use of legumes to meet the protein requirement. Cooked pork, lamb, beef and peas and some combinations of peas and the meats were compared with whole egg as sources of protein for growth in young rats. Measured by growth rate and by efficiency the various meats, when fed at a 10 per cent protein level, were as good sources of protein for growth as were eggs. Cooked peas alone were a poor source of protein for growth. When peas were supplemented with 0.3 per cent dl-methionine, growth was increased until it was not significantly different from that obtained with whole egg protein, although it was not as efficient. At the levels of meat fed in combination with peas, growth was improved over that from peas alone, but even the meat and pea diets were inadequate, as evidenced by a characteristic liver involvement and early death of many of the test animals.

Maine Medical Association Journal, Portland

38:97-118 (May) 1947

Group Practice and Changing Professional Relations in the Hospital. F. T. Hill.—p. 97.
Delayed Obstetrical Labor. K. A. Loughlin.—p. 100.
*Maternal Pulmonary Embolism by Amniotic Fluid: Report of a Case. I. I. Goodof.—p. 101.

Maternal Pulmonary Embolism by Amniotic Fluid.—Goodof's patient, a woman aged 40, had had six previous normal deliveries. This time labor began seven hours after rupture of the membranes and terminated in spontaneous delivery of a dead baby, apparently strangled by the cord. Two hours following delivery the patient began to cough and wheeze. Cyanosis developed and was not relieved by oxygen, morphine and atropine. Respiration became more difficult, and the patient died. At necropsy the lungs were found to be wet. Numerous blocks of lung were fixed for sections. The pulmonary arterioles were massively distended with plugs of epithelial squamae, mucus, meconium and numerous polymorphonuclear leukocytes and lymphocytes. The appearance was identical with that seen in the sediment from amniotic fluid. Goodof thinks that embolism of amniotic fluid explains some cases of unexpected postpartum death. He cites reports by Steiner and Lushbaugh in 1941 of cases of pulmonary embolism by amniotic fluid.

Michigan State Medical Society Journal, Lansing

46:257-376 (March) 1947

Management of Strabismus. E. L. Cooper.—p. 305.
Hypertensive Heart Disease. F. D. Murphy.—p. 310.
Some Clinical Disturbances of Endocrine Glands. E. H. Ryneerson. —p. 318.
Varicose Veins: Observations on Management and Mismanagement. J. A. Witter.—p. 321.
Local Tonsillectomy. H. T. E. Munson.—p. 325.
New Concepts of Causes of Asthma. F. M. Rackemann.—p. 328.

Missouri State Medical Assn. Journal, St. Louis

44:241-312 (April) 1947

Symposium on Fractures:
Some Points in Organization of Rural Hospital Fracture Service. W. J. Stewart.—p. 257.
Colles Fracture. N. Pickard.—p. 258.
Fractures About Elbow Joint. D. L. Yancey.—p. 262.
Fractures of Hip. W. R. Bohne.—p. 267.
Treatment of Simple Fractures of Ankle. J. A. Key.—p. 270.

44:313-384 (May) 1947

Sarcoma of the Soft Parts. A. P. Stout.—p. 329.
Tumor Seminar. A. P. Stout.—p. 334.
Case of Micrococcphilic Hemolytic Staphylococcus Infection of a Pilonidal Dimple. R. Hackmeyer and E. L. Beyer.—p. 344.

New England Journal of Medicine, Boston

236:457-492 (March 27) 1947

Meaning of the Patient to the Hospital. Ida M. Cannon.—p. 457.
Voluntary Hospital: How Can It Survive in Modern World? N. W. Faxon.—p. 460.
Possible Role of Community Hospital in Graduate Training in Surgery. G. Glenn.—p. 464.
Arthritis in Mediterranean Theater of Operations: Clinical Description of Infectious and Other Types of Arthritis. C. L. Short.—p. 468.
Diabetes Mellitus. E. P. Joslin.—p. 474.
Rheumatic Heart Disease, with Severe Mitral Stenosis: Cardiac Hypertrophy, Marked, Right Ventricle.—p. 481.
Glioblastoma Multiforme, Right Temporal Lobe.—p. 487.

236:493-522 (April 3) 1947

Problem of Social Medicine: Equilibrating the Distribution and Technology of Medical Care. W. Carlton.—p. 493.
Teaching Hospital's Service to the Public. A. M. Butler.—p. 497.
*Acute Yellow Atrophy Following Cinchophen Administration: Report of a Case. A. R. Lezzner, L. M. Lockie and C. F. Becker.—p. 500.
*Leukemia Cutis: Report of a Case, with Discussion of Treatment by the Use of Hormones. W. H. Robey and G. G. Russell.—p. 505.
Effects of Protein Deficiency on Pregnant Woman and Fetus and on Infant and Child. H. C. Stuart.—p. 507.
Benign Giant Cell Tumor of Coccyx and Sacrum.—p. 513.
Fibromyxosarcoma.—p. 515.

Acute Yellow Atrophy Following Cinchophen Administration.—Lezzner and his associates observed the development of acute yellow atrophy in a woman aged 39 the day after the ingestion of 2 Gm. of cinchophen; she died twelve days later. The gross and microscopic findings in the liver differed in some respects from those reported in cases of acute or fulminating hepatitis. Clinical and pathologic evidence of preexisting hepatic disease was absent. There was urinary suppression and early phosphorus retention. In addition to the usual picture of cholemic nephrosis the kidneys showed considerable amounts of calcium within the collecting tubules and their peripheral branchings. The authors point out that the first case of acute yellow atrophy allegedly due to cinchophen was reported about twenty years ago and, although similar cases have been recognized since that time, clinicians who use cinchophen with no observed untoward effects have minimized it as a hepatotoxic agent.

Leukemia Cutis.—In the case reported by Robey and Russell the intense skin involvement began early; the leonine appearance of the face and general leukemic infiltration of the skin led to the diagnosis of leukemia cutis—a rare manifestation, only 4 cases having been seen at the Boston City Hospital in twenty years. Two biopsies early in the disease showed the leukemic lymphocytic infiltration of the lesions. Treatment with navital (fish liver oils) and roentgen radiation having proved ineffective, it was decided to try estrogenic substance, first progynon B, with the addition of diethylstilbestrol later. Under this treatment the symptoms diminished, to increase again when the endocrine therapy was interrupted. The patient, a man aged 51, died suddenly with symptoms that suggested pulmonary embolus. Microscopic examination of the skin showed that the corium was extensively infiltrated by lymphocytes, a typical leukemia reaction. The remainder of the picture was consistent with lymphatic leukemia.

Public Health Reports, Washington, D. C.

62:413-448 (March 21) 1947

Simplified Appraisal of Dental Health Programs. J. W. Knutson, Cecelia Mosby and W. A. Jordan.—p. 413.
Shadowed Replicas of Ground Sections Through Teeth. D. B. Scott and R. W. G. Wyckoff.—p. 422.
*Effect of Topically Applied Sodium Fluoride on Dental Caries Experience: IV. Report of Findings with Two, Four and Six Applications. J. W. Knutson, W. D. Armstrong and F. M. Feldman.—p. 425.

Effect of Topically Applied Sodium Fluoride on Dental Caries.—Knutson and his associates present data on the incidence of dental caries in the permanent teeth of three groups of Rochester, Minn., school children who received two, four and six applications respectively of 2 per cent sodium fluoride solution to the teeth in half the mouth. The incidence of initial caries in permanent teeth which were noncarious at the time of treatment was 9.3, 20.1 and 21.3 per cent less in teeth treated with two, four and six applications of fluoride solution respectively than in untreated teeth. The numbers of additional permanent tooth surfaces which became carious in teeth which were carious at the time of treatment were 16.2, 9.6 and 22.2 per cent less in fluoride treated carious teeth given two, four and six applications respectively than in untreated carious teeth.

62:449-484 (March 28) 1947

*Use of DDT to Control Murine Typhus Fever in San Antonio, Texas. D. E. Davis.—p. 449.
Plague: Survival of Infection in Fleas or Hibernating Ground Squirrels. F. M. Prince.—p. 463.

62:485-524 (April 4) 1947

Tuberculosis Mortality in the United States and in Each State: 1945. Elizabeth H. Pitney.—p. 497.
Adapter for Processing 70 mm. Roll Film in Open Tanks. A. J. Mem. —p. 512.

62:525-564 (April 11) 1947

Effects of DDT Mosquito Larviciding on Wildlife: Effects on Surface Organisms of Routine Hand Application of DDT Larvicides for Mosquito Control. C. M. Tarzwell.—p. 525.

DDT in Control of Murine Typhus.—Davis describes the results of an experimental program in San Antonio designed to reduce the number of cases of typhus by controlling the fleas on rats. Previous experiments had shown that the application of DDT to rat runs, burrows and harborages reduces the number of fleas found on the rats. It remained to determine whether the number of cases of typhus can be diminished by dusting DDT in buildings of cities or towns. In the experimental area 20 cases occurred between May 21, 1944 and April 4, 1945, when dusting began. After the program started, 4 cases occurred in treated premises and 10 cases occurred in premises not yet treated. The author concludes that the reduction of rat fleas by distribution of DDT is an additional method for the control of typhus.

Rocky Mountain Medical Journal, Denver

44:257-344 (April) 1947

Rehabilitation of the Deafened. N. Canfield.—p. 275.
Methods of Bringing and Holding Doctors in Rural Areas. F. A. Humphrey.—p. 283.
Carcinoma of Jejunum. K. C. Sawyer, C. W. Workman and F. B. Queen.—p. 287.

South Carolina Medical Assn. Journal, Florence

43:93-126 (April) 1947. Partial Index

Suggestion for Treatment of Chronic Sinus Disease. R. W. Hanchel. —p. 93.
William Henry Johnson, M.D.: A Memoir. J. A. Siegling.—p. 95.

Southern Medical Journal, Birmingham, Ala.

40:281-368 (April) 1947. Partial Index

Roentgen Examination of Sphenoidal Fissures. G. J. Baylin and H. D. Kerman.—p. 281.
Repairing Bone Defects in Cranium and Tibia. J. R. Green.—p. 289.
Technical Considerations in Adequate Transurethral Prostatic Resection. A. F. Turner Jr., L. M. Orr and J. C. Hayward.—p. 296.
Diverticulosis Coli with Coexisting Carcinoma of Rectosigmoid: Report of 2 Cases. B. G. Oren.—p. 304.
Fractures of Pelvis: Study of End Results. R. L. Anderson and H. M. Hills Jr.—p. 308.
Abortions Treated Conservatively: Twelve Year Study Covering 3,739 Cases. P. B. Russell Jr.—p. 314.
Some Effects of Posture on Patients During and After Operation. R. J. Fornataro.—p. 324.
*Present Evaluation of Response of Prostatic Cancer to Hormone Therapy. C. L. Deming.—p. 328.
Lack of Response to Insulin: Report of Patient Treated with 5,000 Units per Twenty-Four Hours. L. S. Smelo.—p. 333.
Acute Hepatitis in Children: Clinical Features and Laboratory Tests. C. H. Webb, S. G. Wolfe, R. T. Lucas and C. E. Anderson Jr. p. 340.
*Narcosynthesis in Civilian Practice. J. S. New and A. R. Kelly Jr. —p. 349.

Response of Prostatic Cancer to Hormone Therapy.—Deming applied hormone treatment by giving diethylstilbestrol orally, by castration or by a combination of castration and diethylstilbestrol. Synthetic estrogen therapy is of equal and perhaps of more value than castration. When the primary and distant metastatic lesions respond they do so regardless of the method of hormonal application. Dosage of estrogen should be determined on the basis of symptoms, rectal findings, x-ray evidence of osteoplastic activity and acid phosphatase readings. It is just as judicious to apply hormonal therapy early for prostatic cancer as it is to apply any other form of cancer therapy early for other forms of cancer. Synthetic estrogen treatment should be continued as long as the patient lives, whether castration has been done or not. The only known cure for cancer of the prostate is early radical prostatectomy, before it has become a biologic cancer and disseminated to periprostatic and distant organs.

Narcosynthesis.—In narcosynthesis barbiturates are administered intravenously as a means of facilitating psychotherapy. New and Kelly used this method in about 300 cases of acute war neuroses and a similar number of civilian cases with a wide range of disorders usually classed as psychoneurotic or psychosomatic. They gained the impression that narcosynthesis is of great value. Many patients obtain relief in a few days. With many others the period of treatment, although somewhat longer, is substantially shorter than if other methods are used. Narcosynthesis is one of the most practical and useful methods available in psychiatry, particularly with noninstitutionalized patients.

Western J. Surg., Obst. & Gynecology, Portland, Ore.

55:209-262 (April) 1947

Preservation of the Upper Pelvic Floor and Bladder Support in Total Hysterectomy. G. E. Judd.—p. 209.
Report on Experience with Vaginal Hysterectomy. H. C. Stearns. —p. 220.
Present Status of Prostatic Resection. L. Smith and H. L. Chambers. —p. 236.
Rh Factor: Present Status and Clinical Importance. D. B. Rice.—p. 238.
Recent Advances in Neurosurgery. F. M. Anderson.—p. 245.

55:263-312 (May) 1947

Primary Ovarian Malignancy. J. V. Campbell and D. Siegman.—p. 263.
Degenerating Tumors Complicating Pregnancy Myomectomy in the Prenatal Period. E. F. Anderson.—p. 273.
Psychoneurogenic Causes of Sterility and Their Treatment: Preliminary Remarks on Allergenic Sterility. J. J. Rammer.—p. 278.
Late Pregnancy Toxemia: Review of Experimental Findings. G. V. S. Smith and O. W. Smith.—p. 288.
Report of Primary Torsion of the Right Fallopian Tube. M. A. Howard. —p. 295.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

Archives of Disease in Childhood, London

21:181-240 (Dec.) 1946

Height and Weight in Relation to Onset of Puberty in Boys. R. W. B. Ellis.—p. 181.
Observations on Growth of Children. G. M. Allen-Williams.—p. 199.
The Blood in Infancy. L. Findlay.—p. 195.
Biliary Obstruction Associated with Icterus Gravis Neonatorum. R. Lightwood and M. Bodian.—p. 209.
Etiology of Intermittent Esophageal Regurgitation and Hematemesis in Infants. W. G. Wyllie and C. Elaine Field.—p. 218.
Observations on Hemolytic Disease of Newborn. R. R. Gordon.—p. 225.
Treatment of Erythroblastosis Fetalis. I. A. B. Cathie.—p. 229.
Plasma Volume in Nephritis. P. MacArthur.—p. 235.

Australian J. Exper. Biol. and M. Science, Adelaide

26:253-336 (Dec.) 1946. Partial Index

*Passive Immunization by Intranasal Route in Experimental Pertussis. E. A. North.—p. 253.
Modified Salk Test for In Vitro Titration of Influenza Antibodies. S. G. Anderson, F. M. Burnet and Joyce D. Stone.—p. 269.
Inhibitory and Inactivating Action of Normal Ferret Serums Against an Influenza Virus Strain. F. M. Burnet and J. F. McCrea.—p. 277.
Nonspecific Serum Inhibition of Influenza Hemagglutination. J. F. McCrea.—p. 283.
Aspects of Immunology of Rh Factor. P. M. de Burgh, Ruth A. Sawyer and R. J. Walsh.—p. 293.
Factors Influencing Virulence of Hemophilus Pertussis Phase I. D. F. Gray.—p. 301.
Accommodation of Nerve in Myasthenia Gravis and in Partial Curarization. E. L. Stratmann, R. D. Wright and G. Reid.—p. 313.

Intranasal Administration of Pertussis Antiserums in Mice.—According to North, mice have been shown to be suitable for the study of immunity in pertussis. Evans observed in 1944 a protective action of absorbed pertussis antiserum given to mice intranasally together with the infecting doses of Hemophilus pertussis. Evans concluded that both pertussis antibacterial serum and pertussis antitoxin are able to protect mice against infection by H. pertussis. North describes experiments carried out in an effort to confirm and extend Evans's observations. A high degree of protection against subsequent lung infection in mice is given by intranasal injection of pertussis antiserums. A lesser degree of protection is obtained when the serum is given after intranasal infection with H. pertussis. An absorbed human antibacterial serum protects mice better than a similarly absorbed antitoxic serum.

British Journal of Industrial Medicine, London

3:207-282 (Oct.) 1946

Toxicology of the Newer Metals. L. T. Fairhall.—p. 207.
Poisoning of Firemen by Irritant Fumes: Cadmium and Sulfonated Castor Oil. D. O. Shiels and I. Robertson.—p. 213.
Transfer of Heat Through Sun Helmets. P. S. H. Henry and W. H. Rees.—p. 225.
Experiment on Use of Psychologic Tests as Aid to Rehabilitation of Hospital Patients. Alice W. Heim and Audrey Reasinos.—p. 237.
Acute Paranitraniline Poisoning. A. Anderson.—p. 243.
*Occupational Hazard of DDT Spraying. I. Gordon.—p. 245.
Oleogranuloma: Late Effects of Accidental Injection of Mineral Oil Under Pressure. B. Moore.—p. 250.
Calcium Necrosis of the Skin. A. G. Hoppleston.—p. 253.

Occupational Hazard of DDT Spraying.—Gordon had an opportunity to investigate the toxic action of DDT in the field on a team of Africans who were occupied with spraying on five days of each week. Instructions were issued for personal protection against possible absorption by the wearing of gloves, gas capes and eye shields and for provision of an anti-drip can on the Mackenzie sprayer to catch the large amount of spray that ran back from the nozzle on to the operator's hands. However, no amount of ordering would convince these African civilians of the necessity for precautions. Blood examinations, regular weighings and skin inspections revealed that, although, these men were probably undernourished and took no precautions against skin absorption, no signs or symptoms of DDT poisoning were found. Slight increases in the leukocyte count were noted. When DDT was used in kerosene, rashes were common when sprayers first started on the work. After some months, however, they became desensitized. By means of a patch test it was shown that the irritation is primarily due to the kerosene and made considerably worse by the DDT dissolved in it. DDT alone is innocuous. A plea is made for the discontinuance of kerosene as a solvent for DDT.

British Medical Journal, London

1:437-476 (April 5) 1947

Pethidine in Labor: Results in 500 Cases. Josephine Barnes.—p. 437.
Outbreak of Staphylococcal Food Poisoning. J. G. Oddy and H. W. Clegg.—p. 442.
d-Tubocurarine in Cesarean Section. T. C. Gray.—p. 444.
*Use of d-Tubocurarine Chloride and Thiopentone in Electroconvulsion Therapy. J. A. Hobson and F. Prescott.—p. 445.
Use of Curare in "Poor Risk" Patients. G. Outlere.—p. 448.
d-Tubocurarine Chloride in Electroconvulsion Therapy. A. Gillis and D. D. Webster.—p. 451.

d-Tubocurarine Chloride and Thiopentone in Electric Convulsion Therapy.—Hobson and Prescott describe the use of d-tubocurarine chloride and thiopentone for modifying electrical convulsions in 50 patients undergoing treatment for psychiatric illness. In all, 300 treatments were given. These drugs do not significantly affect the electrical convulsion threshold. The advantages claimed for the method are that the traumatic complications of electric convulsion therapy are avoided, there is no serious rise in blood pressure, it enables electric convulsion therapy to be given to certain patients in whom otherwise convulsions would be contraindicated, postconvulsive excitement is minimized, the procedure can be carried out single handed if desired and the unpleasantness of electric convulsion therapy for the patient is almost entirely eliminated.

1:477-516 (April 12) 1947

Study of Surgical Anatomy of Vagina, with Special Reference to Vaginal Operations. W. Shaw.—p. 477.
*Treatment of Reiter's Syndrome by Gold Salts. R. R. Willcox, G. M. Findlay and A. Henderson-Begg.—p. 483.
Serum Typhus Vaccine: Effect on 16 Cases Incubating the Disease. W. T. Walker.—p. 484.
Prognosis of Primary Pleurisy with Effusion. B. C. Thompson.—p. 487.
Case of Bilateral Simultaneous Spontaneous Pneumothorax. G. M. Komrower.—p. 488.

Gold Salts in Reiter's Syndrome.—Willcox and his associates point out that in experimental animals certain strains of pleuropneumonia-like organisms give rise to arthritis and conjunctivitis. An attempt was made to isolate pleuropneumonia-like organisms from the conjunctiva and joint fluids of patients with Reiter's disease. Two patients with arthritis and urethritis, one of them also with conjunctivitis, have been investigated for the presence of pleuropneumonia-like organisms by culture of the joint fluid and blood on suitable mediums rich in animal protein and by inoculation of blood and joint fluid into mice. Apart from the production of arthritis in a single mouse by the injection of joint fluid from one patient, an investigation of 2 patients with Reiter's syndrome was negative for the presence of pleuropneumonia-like organisms. Since pleuropneumonia-like organisms have shown sensitivity to gold salts, injection of such salts was resorted to in 2 patients with Reiter's syndrome. This treatment was curative, while penicillin and sulfonamides were of little value.

J. of Neurol., Neurosurg. and Psychiatry, London

9:81-112 (July) 1946

Chronic Progressive Ophthalmoplegia of Myopathic Origin. P. H. Sandifer.—p. 81.
*Paget's Disease of Atlas and Axis. N. Whalley.—p. 84.
*Effects of Vitamin and Hormone Treatment on Senile Patients. P. E. Vernon and M. McKinlay.—p. 87.
Nerve Biopsy. W. Holmes and R. B. Zachary.—p. 93.
Pattern of Olfactory Innervation. W. E. Le Gros Clark and R. T. T. Warwick.—p. 101.

Paget's Disease of Atlas and Axis.—Whalley says that, although Paget's disease commonly affects the vertebral column, it is rare for it to result in interference with spinal cord function. In an extensive search of the literature on the subject of spinal cord complications secondary to osteitis deformans the author has been unable to find any instance of the disease affecting the atlas and axis vertebrae and causing spinal cord compression. In the case described here, not only had the disease process produced cord compression, but it had also resulted in spontaneous forward dislocation of the head on the

cervical spine. The patient was a man aged 66. The x-ray illustrates massive new bone formation, fusion of the vertebrae, kyphosis and dislocation of the head. Narrowing of the spinal canal can also be seen. The postmortem specimen shows encroachment of the bony overgrowth on the spinal canal and its contents.

Effects of Vitamin and Hormone Treatment on Senile Patients.—Vernon and McKinlay treated small groups of senile patients with vitamins B and C and with androgenous hormones. The patients, together with similar numbers of untreated controls, were tested individually with mental and psychomotor tests before treatment and during each phase of treatment. No evidence was obtained of any general improvement in intellectual efficiency or psychomotor capacities as a result of treatment. The only positive psychologic findings of this investigation were that moderate doses of vitamins may improve general mental ability among severe cases of senility, and may produce some increase in fluency and decrease in perseveration among light and moderate cases. Even these changes, amounting to about 10 per cent, are so much on the borderline of statistical significance that they cannot be regarded as proved without further evidence.

Lancet, London

1:471-506 (April 12) 1947

*Outbreak of Virus Encephalomeningitis in Northwest Middlesex. G. H. Gennings.—p. 471.
Continuous Injection of Penicillin: Secunderabad Apparatus. J. H. Bowie and M. D. Bovear.—p. 477.
Mammary Cysts: Their Treatment. F. C. Pybus.—p. 480.
*Scrub Typhus Vaccine: Field Trial in Southeast Asia. W. I. Card and J. M. Walker.—p. 481.
Epilepsy and Hysteria. D. N. Parfit.—p. 483.
Modification of Human Red Cells by Virus Action: Agglutination by "Incomplete" Rh Antibody. C. M. Chu and R. R. A. Coombs.—p. 484.

Outbreak of Virus Encephalomeningitis.—An outbreak of neurotropic virus infections in which meningitic and encephalitic symptoms were prominent was observed between March and November 1946. In this outbreak 22 patients with meningitis or encephalitis and 13 with less clear signs and symptoms were admitted to the hospital. The cases occurred chiefly during the summer. In no case was it possible to trace a direct contact with another case in the family, school or work place. One peculiar coincidence was the admission of case 11 on the same day as a classmate who had clinical poliomyelitis. When the cases of encephalomeningitis were seen, an outbreak of poliomyelitis existed in the region and Brodie's statement that half the poliomyelitis cases in an epidemic are nonparalytic might suggest that the cases seen by the author were atypical forms of poliomyelitis. Most of the cases involved children or young adults. The illness usually began suddenly with fever and frontal headache. Though meningitic manifestations (headache, vomiting, photophobia and stiffness of the neck) were almost constant at this stage, they were sometimes not well defined. After admission the course of the illness was variable, but in most cases there was fever for about a week, and in many cases it was of low grade. Paul-Bunnell and Widal tests, done in some cases, were negative. Treatment appeared to have little effect. The weight of evidence is against these cases being due to an injection by the virus of Armstrong and Lillie. Whether one or more viruses were responsible for the infections also remains to be shown. The well known variations in the cerebrospinal fluid findings and the clinical picture, even in a recognized infection such as Armstrong's virus, and the number of neurotropic viruses as yet not isolated, make exact diagnoses difficult.

Scrub Typhus Vaccine.—Card and Walker say that with the realization in 1943 that scrub typhus would form a major medical problem in the war in Southeast Asia, work was started on the production of a vaccine. They describe a field trial with scrub typhus vaccine. Between July 1945 and February 1946 sufficient vaccine was distributed for the vaccination of over 60,000 men, though only 10,000 of these were inoculated on a controlled basis. As recommended by the Medical Research Council, 1 cc. of vaccine was given on three occasions at weekly intervals. No reactions were observed. There were 9 cases of scrub typhus in fully protected persons and 24 in partially protected persons. It is impossible on the limited evidence to say whether or not the vaccine has any effect on the mortality or incidence of the disease. The available evidence suggests that the vaccine has no noticeable effect on the clinical course or serologic reactions of scrub typhus.

Bruxelles-Médical, Brussels

27:555-620 (March 16) 1947

*Mortality Rate of Appendicitis in Switzerland. S. Cuendet.—p. 565.
Contribution to Study of Fibromyoma of Cervix of Uterus. Bourg and Hannes.—p. 577.

Appendicitis in Switzerland.—The operative mortality rate of appendicitis in Switzerland was reduced progressively from 21 per cent at the end of the last century to 6 per cent in 1912, to 3 per cent in 1937 and to 1 per cent and even to less at present. The absolute mortality showed a pronounced increase up to 1937 in spite of the percental reduction of the operative mortality. Since that date up to 1944 the mortality has been reduced regularly. From 530 fatalities in 1937 it was reduced to 315 in 1944 in spite of the unfavorable conditions due to the mobilization of the army. According to Cuendet early diagnosis and early surgical intervention and better information passed on to the public may be responsible for this reduction, which preceded the introduction of the sulfonamides. In 1945 there was a mild increase of the mortality in spite of the use of penicillin, which became general in Switzerland in the spring of 1945. Three hundred persons are still dying from appendicitis in Switzerland yearly, with the majority of patients between the ages of 5 and 15; there is a progressive reduction of mortality in the next age groups and again an increase in the mortality of patients between the ages of 55 and 70 years. A critical study of 68 fatal cases from civilian life and from the federal military insurance revealed that in 51 death resulted from generalized peritonitis or from intestinal occlusion and in 15 per cent of the military cases from pulmonary embolism. In more than 50 per cent of the fatal cases operation was performed too late through their own fault or the fault of the family or because of difficult diagnosis. Obligatory preventive appendectomy in childhood does not seem feasible for the country as a whole, but individual preventive appendectomy is suggested, although one should keep in mind that it is not always without a risk.

Paris Médical

1:97-112 (March 1) 1947

Diseases of Respiratory Apparatus in 1947. M. Baridy and R. Laubry.—p. 97.
Alveolar Exudation and Bronchial Excretion. P. Ameuille.—p. 103.
Incidents and Accidents of Bronchoscopy in Patients with Pulmonary Tuberculosis. C. Gerson-Rieux, A. Breton and J. Mevrou.—p. 105.
*Treatment of Dyspnea in Asthmatic Patients with Theophylline. J. Turiaf and M. Bourel.—p. 109.

Theophylline in Asthma.—Turiaf and Bourel administered theophylline and theophylline ethylenediamine to 181 patients with asthma. One intravenous injection of 0.25 Gm. of theophylline in the morning and one in the evening, and one 0.35 Gm. theophylline suppository at noon brought radical relief of dyspnea in five to ten minutes after the injection and in fifteen to twenty minutes after the introduction of the suppository. This treatment was effective in 150 patients, 108 of whom had isolated paroxysmal attacks, while 38 had continuous dyspnea and 4 had effort dyspnea. Theophylline was effective in cases of severe asthma of ten years' duration in which pituitary-epinephrine preparations as well as procaine hydrochloride were ineffective. Untoward reactions did not develop. Thirty-one patients were failures, 25 of whom had continuous dyspnea and 6 had effort dyspnea. It is suggested that the highly satisfactory results obtained with theophylline may be partly due to its effect on the vasomotor apparatus of the epithelial lining of the bronchi.

Minerva Medica, Naples

38:201-220 (Feb. 17) 1947. Partial Index

*Heart and Hypovitaminosis B_1 in Pregnancy. F. De Matteis and E. Robecchi.—p. 201.

Heart and Hypovitaminosis B_1 in Pregnancy.—Twenty multiparous women with cardiac symptoms during the third and fifth months of pregnancy were given daily intramuscular or intravenous injections of from 20 to 30 mg. of vitamin B_1. Con-

trol of the subjective symptoms, return to normal pulse and disappearance of headache, edema and stenocardiac crises was obtained in the 13 patients who followed the treatment for one or two weeks. The failure in 7 patients was due to lack of cooperation and insufficient therapy.

Arch. Ital. d. Mal. d. App. Diger., Bologna

13:3-65 (Jan.) 1947. Partial Index

*Primary Isolated Lymphogranulomatosis of Stomach. F. Farnesi.—p. 3.

Lymphogranulomatosis of Stomach.—A man aged 38 had symptoms of gastric ulcer. He was in poor nutritional condition when the first vomiting of blood occurred. Four days later the second vomiting took place. It was profuse and caused his death. Necropsy showed fibrous fat infiltration of the stomach (especially the antral region), zones of necrosis and enlarged peripancreatic and perigastric lymph glands. The histologic diagnosis was lymphogranuloma.

Prensa Médica Mexicana, Mexico, D. F.

12:1-26 (Jan. 31) 1947. Partial Index

*Infantile Poor Nutrition in Mexico. F. de P. Miranda.—p. 1.

Undernourishment of Infants in Mexico.—Undernourishment of infants and children of poor families dates back to remote epochs before the discovery of America. The most acute period is that of weaning, which is followed by chronic undernourishment up to the age of 6 years. The mortality from infancy to the age of 6 years is high. Clinically there is a lack of proteins as the causal factor of disorders of somatic development, disorders of the type of fatty liver, diarrhea, a tendency to frequent infections, dehydration, edema and sometimes pellagra, ariboflavinosis and xerosis.

Revista de la Asoc. Méd. Argentina, Buenos Aires

60:677-724 (Aug. 15) 1946. Partial Index

*Subacute Lymphoid Leukemia in Chronic Pulmonary Tuberculosis. I. M. Hernández and I. Smirnoff.—p. 677.

Lymphoid Leukemia in Pulmonary Tuberculosis.—The subject of this report, a man aged 30, presents the first instance of subacute lymphoid leukemia occurring in chronic pulmonary tuberculosis and the third instance of leukemia seen in the Hospital Tornú of Buenos Aires. The pulmonary tuberculosis was latent. The pathogenesis of lymphoid leukemia is not definite. In the reported case the clinical form was that of subacute lymphoid leukosis. Blood transfusions, sedatives and vitamins did not modify the course of the disease. Intercurrent bronchopneumopleuropathy was the immediate cause of death.

Revista Española de Tuberculosis, Madrid

18:7-90 (Jan.) 1947

*Bronchiectasis in Children. S. A. Ayerbe Valles.—p. 11.
Myocardial Infarct in Adolescents. A. Crespo Alvarez and J. Márquez Blasco.—p. 39.

Bronchiectasis in Children.—Ayerbe Valles reports 13 cases of bronchiectasis in children between the ages of 7 and 12 years. Pleuritis, tuberculous adenopathies and tuberculous infiltration are the etiologic factors which bring about partial bronchial obstruction and local retention of secretions. The effect of atelectasis is indirect. The role of a congenital factor is possible. Blood spitting is an early symptom. Typical clinical symptoms manifest themselves in advanced periods. When a definite diagnosis cannot be made from a roentgenogram, x-ray examination after injection of iodized oil is indicated.

Bibliotek for Laeger, Copenhagen

138:261-272 (Dec.) 1946

*Factors Affecting Mortality in Operation for Gastric or Duodenal Ulcer Without Acute Complications. J. L. Hansen, A. Berbie, H. B. Rasmussen and E. Rasjen.—p. 261.

Mortality in Operations for Gastric or Duodenal Ulcer.—Analysis of 531 cases in which operation was performed for ulcer without acute complications in three districts in Denmark during the last ten years, Hansen and his associates state, shows that of the factors which affect the mortality and can be influenced preoperatively the hemoglobin percentage, weight and stomach retention are especially important. If stomach retention cannot be overcome the prognosis is less favorable; gastroenterostomy may have to be done instead of resection. In underweight patients resection seems to be performed too often in proportion to gastroenterostomy. The factors which depend on how early and how often operation is done are of more basic importance in the question of mortality. The present work is an argument for earlier and more frequent operation. If there are repeated periods of increased activity, perhaps bleeding or perforation, if loss of weight and anemia occur, or achylia and retention, if the ulcer by x-ray manifests itself more clearly, and if rational medical treatment cannot cause the symptoms definitely to disappear, operation is advised. Before operation all means must be used to bring weight and hemoglobin count to normal and keep them so for a longer time, so that eventual general cell injuries can be repaired before the intervention. If these lines of guidance were followed a far larger number of ulcer patients would be operated on, considerably more milder cases and relatively fewer grave cases would be included, and a decline in the absolute number of grave ulcer cases would gradually follow.

Nordisk Medicin, Gothenburg

33:283-350 (Jan. 31) 1947. Partial Index

Treatment of Ulcer Disease. T. Andersen.—p. 283.

Hospitalstidende

*Spinal Anesthesia with Nupercaine According to Sebrecht. H. Fiil.—p. 291.
Encephalitis Following Measles. Emma Vestergaard.—p. 296.
Congenital Megacolon. H. Meltrup Poulsen.—p. 299.

Finska Läkaresällskapets Handlingar

Narcosis in Operations for Goiter. T. Sandelin.—p. 307.
Postoperative Parotitis. R. Jäps.—p. 309.
Polycythemia, Anemia and Calcified Spleen in Same Patient. J. Porsell.—p. 313.

Hygiea

*One Hundred Positive Hypoxemia Tests. G. Bürck and R. Pauelov.—p. 315.
Vitamin C in Infancy. Irma Vitolin and L. Hesselvik.—p. 323.

Spinal Anesthesia with Nupercaine.—Fiil says that this form of spinal anesthesia gives definite effect for a longer period than do other forms and is therefore recommended for supraumbilical laparotomies. Of the 916 cases reported, 639 were supraumbilical and 277 infraumbilical. There were no anesthetic deaths. Collapse occurred in 18 patients but they all recovered. Jaundiced patients seem to be more liable to collapse after high spinal anesthesia. Injection of ecophedal does not affect the occurrence of collapse but apparently aggravates its course. Collapse is independent of the amount of nupercaine used. Prophylactic injection of ephedrine is of no value. Two patients were refractory to the anesthetic. In 18 cases the anesthesia had to be supplemented with inhalation narcosis; 12 of these cases, also 12 of the collapse cases are ascribed to insufficient experience on the part of the anesthetist. The anesthetist should become apprehensive when the patient coughs, sneezes or is nauseated, as increased intra-abdominal pressure will cause the anesthesia to rise faster than intended.

Hypoxemia Tests.—The test was made on 666 patients, 378 men and 288 women. Of the 100 positive tests 40 were in men and 60 in women. Seventeen were in patients without suspected coronary disease, 53 in patients with suspected and 30 in patients with probable or certain coronary disease. Study of the positive tests shows a relative preponderance of women and a relative preponderance of patients with hypertension, especially in patients without suspected coronary disease. Positive tests in both men and women were more common in persons with heart of normal size than in persons with enlarged heart. In persons with enlarged heart an increased venous stasis in the coronary circulation may perhaps favor the development of collaterals. Seventeen patients, 16 of whom were women, are designated as neuropathic. While the hypoxemia is still considered a test of the function of the coronary circulation, a positive outcome does not necessarily mean organic disease; in some instances it is probably an indication of functional disorder.

Book Notices

Allergy in Theory and Practice. By Robert A. Cooke, M.D., Sc.D., F.A.C.P., Attending Physician and Director of the Department of Allergy, the Roosevelt Hospital, New York City, in Association with Herman B. Baldwin, and others. Cloth. Price, $8. Pp. 872, with 44 illustrations. W. B. Saunders Co., W. Washington Square, Philadelphia 5, 1947.

The author is a pioneer in the field of allergy, and this volume represents his experience and his teaching during more than thirty years. The book covers the theoretical and clinical aspects of the various allergic diseases, together with allergic factors in rheumatic fever, glomerulonephritis, tuberculosis and lupus erythematosus. A large part is given over to the fundamental aspects of allergy. The various theories regarding anaphylaxis, allergy and immunity are analyzed with great care. The role of histamine or some H-substance is discussed, but the author correctly points out that "actually there is as yet no convincing and confirmed proof that H-substance is liberated in the allergic wheal."

Much attention is given to serologic features of the immediate wheal-reacting allergies, pathologic-anatomic aspects of allergy and immunochemistry of antigens and antibodies. The various allergic conditions are then discussed individually, and this is followed by chapters on allergy due to bacteria, inhalants, foods, drugs, endocrine products, serum and physical allergy. There is also a chapter on skin testing and one on laboratory procedures.

Most of the book is by Dr. Cooke, but chapters also are written by thirteen associates. Asthma is divided into non-infective and infective, and a small but excellent concise pharmacopeia is attached. Morphine or other opium derivatives are advised in the treatment of severe bronchial asthma. Most allergists are strongly opposed to this advice; they have seen too many fatalities follow within a few hours after the needle has been inserted. Throughout the book runs the infection motif, this factor in allergy being more strongly stressed by the author than by most other allergists. This does not imply that the author is wrong. Cooke is almost certainly correct when he insists that true immediate positive whealing skin tests in "eczema" (atopic or intrinsic dermatitis) are not necessarily related to the dermatitis itself; they signify either associated or potential allergies which occur much more rapidly than does "eczema."

The fundamental and theoretical aspects of allergy are concisely stated. No other book is more authoritative in this respect. It summarizes all the important research work to date and points out some of the problems which need investigation. The clinical section of the book is also good but is not as distinctive. It lacks many of the details which would enable general practitioners to cope successfully with difficult allergic problems. Skin testing, according to Spain, one of the co-authors, should be done only by the intracutaneous method. He states (page 109) that "by experience it has been learned that the potencies adopted (of various extracts) are quite safe except for the occasional, exquisitely sensitive person who can usually be identified before testing by points in his clinical history." That this statement leaves something to be desired is shown by continuing case reports of death or anaphylactic shock after intracutaneous skin tests. Much to be preferred is the statement in the same book (page 502) by Walzer, another co-author, that "the scratch test is by far the safer method for the novice who is not fully cognizant of the dangers of testing and of the steps for preventing and counteracting untoward reactions which may result from the procedure." The chapter on migraine, from the standpoint of allergy, has a defeatist point of view; the importance of allergy is belittled, this despite the many reports of complete relief from attacks when the food has been discovered and avoided. Details regarding elimination diets or diet records should be given in this chapter.

The book is strongly recommended to all interested in the field of allergy and is a must for those who are especially concerned with studies of immunology. It is well written, concise, well printed and nicely illustrated. It has many good case reports and references.

Elements of Genetics: Haldane's Laws of Heredity with Special Application to Man. By Edward C. Colin, Ph.D. Second edition. Paperbound. Price, $2.50. Pp. 402, with 99 illustrations. Blakiston Co., 1012 Walnut St., Philadelphia 5, 1946.

This book is attractive in format and generously illustrated with diagrams, drawings and well chosen photographs. The author presents clearly and concisely the principles of heredity. He includes an up to date discussion of cytogenetics, the nature and causes of mutations, the relative roles of environment and heredity, inbreeding and crossbreeding, and factors involved in evolution. The important subject of probability is presented with unusual clarity. The historical material, particularly the contribution of Mendel, is skilfully used as a basis for presenting genetic principles. Fully half of the book is devoted to a discussion of human heredity. Included here are hereditary characteristics of skin, hair, nails, teeth, eyes, skeleton and muscles and of the circulatory, respiratory, excretory, endocrine, digestive, reproductive and nervous systems. Hereditary factors in cancer and other diseases are considered. Examples of human sex-linked factors, those on the X and the Y chromosomes, are given. However, Haldane's interesting work on partially sex-linked factors and his mapping of the homologous section of the X and Y chromosomes are omitted. The medical man will find this book of unusual interest in that it presents clearly the principles of heredity and then shows their application to the human body in health and disease.

The final chapter on improvement of the human species deals with both negative and positive eugenics. Exception might be taken to certain implications concerning immigration laws and the subsidization of families of the so-called fit. However, the analysis of the role of negative eugenics, marriage restrictions, segregation and sterilization in reducing different types of hereditary defects in a country is exceptionally well presented. If carefully studied, the contents of this book could be highly illuminating to those medical practitioners whose training has not included a course in genetics. It is particularly recommended to young men in medicine or intending to enter this field.

La chirurgie en obstétrique. Par R. Keller, professeur de clinique d' obstétrique et de gynécologie à la Faculté de médecine de Strasbourg, et A. Gingibaer. Préface du Pr Boeb. Paper. Price, 220 francs. Pp. 222, with 79 illustrations. Masson & Cie, 120 Boulevard Saint-Germain, Paris 6e, 1946.

This book does not deal with obstetric operations such as forceps deliveries but with surgical procedures for complications that occur during gestation and also with operations for conditions that prevent pregnancy. The authors describe and in most cases illustrate operations for (1) malformations of the genital organs such as imperforate hymen, stenosis of the vagina and cervix, absence of the vagina and double vagina or uterus, (2) acquired sterility due to inflammatory disease, neoplasms and retroflexion, (3) special obstetric conditions which can be remedied by surgical procedures such as ectopic pregnancy, fixed retroflexed gravid uterus, hydatid mole and chorionepithelioma, (4) complications of pregnancy which can be corrected surgically, including appendicitis, intestinal obstruction, cancer of the cervix, fibromyomas of the uterus and ovarian cyst, (5) soft part and bony dystocia at the end of pregnancy and during labor, including cesarean section, symphysiotomy and means of treating placenta previa, abruptio placentae, rupture of the uterus and other conditions, (6) postpartum infections such as uterine abscess, phlebitis, peritonitis and pelvic abscess and (7) noninfectious complications after labor such as inversion of the uterus, vesical and rectal fistulas and perineal lacerations.

A large portion of the book deals with rare conditions, some of which are never encountered even in the lifetime of obstetricians of long experience. The only operations illustrated for constructing a vagina are those of Schubert and Baldwin-Mori, both of which are now obsolete because much simpler and safer operations exist. Likewise, the Braxton Hicks version should be discarded for the treatment of placenta previa. Since this is a book dealing with surgery there should be more illustrations. Nevertheless the book is well written, and the advice given is generally practical and useful. It should be helpful to obstetricians and surgeons who can read French.

Textbook for Psychiatric Attendants. By Laura W. Fitzsimmons, R.N., B.S., M.A., Assistant Director of Nurses, and Chief Neuropsychiatric Nurse, United States Veterans' Administration. Cloth. Price, $3.50. Pp. 282, with 5 illustrations. Macmillan Company, 60 Fifth Ave., New York 11, 1947.

Although this volume is said to be designed for attendants in mental hospitals, the treatment of topics is strongly reminiscent of books of instruction for psychiatric nurses. The vocabulary is occasionally erudite and will not be readily understood by many attendants; e. g. "patients who are cognizant of their surroundings" (p. 148), "interproximal surfaces of the teeth," "upper lingual surfaces" (p. 249). On the other hand, phrases are used which are not in good repute in schools of nursing, such as "a patient is diagnosed as having . . ." (p. 31). It is not good form today to refer to patients as "cases" (pp. 34 and 192) but rather to speak of persons having symptoms or disease conditions. As a textbook it leaves something to be desired. The index is incomplete. The only item which in any way refers to medications is "labels, medicine," although "administration of medicines by mouth" appears on pages 296-299. In view of the importance given today to the use of visual aids as a desirable teaching aid, it is unfortunate that there are no diagrams or illustrations to help the attendant in either the nursing procedures or the management of patients. There should be a considerable demand for a textbook for psychiatric attendants. If the demand meets expectations, the book should be carefully edited to fulfil successfully the requirements of the trainee attendant before the publishing of a second edition.

Early Ambulation and Related Procedures in Surgical Management. By Daniel J. Leithauser, M.D., F.A.C.S., Chief of Surgery, St. Joseph Mercy Hospital, Detroit, Michigan. Cloth. Price, $4.50. Pp. 222, with 38 illustrations. Charles C Thomas, 301-327 E. Lawrence Ave., Springfield, Ill., 1946.

This is a highly personalized account of the experience of one surgeon with early ambulation postoperatively. The author does not claim priority, and indeed, many surgeons have long practiced some form of early rising after operation. This does not mean a shortening of the accepted lengthy stay in bed by a few days but involves a systematic attempt to force (better persuade) even reluctant patients out of bed within a few hours after operation. The advantages of such procedures are now generally recognized and need not be detailed here. Early ambulation has thus become the preventive phase of physical rehabilitation by preventing the debility associated with confinement to bed for any long period. The author outlines briefly some historical features of the technic and the physiologic principles forming the scientific basis for the method. He is a strong advocate of the transverse incision, and the use of steel wire for closure of laparotomy wounds. The particular relationship between these two features, especially the second, and early rising is a matter of some controversy. Most important in the whole scheme is the nursing care. When nurses understand the importance of early ambulation and are properly trained to assist the patient in his first few attempts, the method will be spectacularly successful. This the author emphasizes. The results of his experiences are analyzed and are impressive.

Medical Services by Government: Local, State, and Federal. By Bernhard J. Stern, Ph.D. Studies of the New York Academy of Medicine Committee on Medicine and the Changing Order. Cloth. Price, $1.50. Pp. 288. Commonwealth Fund, Division of Publications, 41 E. 57th St., New York 22; Oxford University Press, Amen House, Warwick Sq., London, E. C. 4, 1946.

This is one of many monographs published in recent years by the Commonwealth Fund under the auspices of the Committee on Medicine and the Changing Order of the New York Academy of Medicine. The author traces briefly the development of governmental responsibilities for medical services from the poor laws of the colony days to the present time. The repressive features of the early poor laws have never quite disappeared from government medical service, particularly at the state and local levels. Local responsibility still prevails and, according to the author, "has led to wasteful multiplicity of small administrative jurisdictions." The assumption by state governments of more and more responsibility in the field of medical services has been instrumental in extending the scope beyond the indigent. Data on expenditures of government agencies for medical services are fragmentary; yet they seem to bear a direct relation to the per capita income of the area. A short but comprehensive picture is given of the extent of government participation in the provision of hospital services. The phenomenal growth in government hospital facilities, the change in public attitude toward such institutions and the resulting demand for more adequate services has brought about a vast federal grants-in-aid program. This program is traced in detail. Considerable discussion is also given over to the medical services traditionally provided by the federal government. Dr. Stern has done an excellent job in tracing the shifting role of the local, state and federal governments in the field of medical care. One of the few criticisms that can be made is that throughout the entire discussion he has dealt with medical care in terms of dollars, facilities, statutes and agencies with too little recognition of the role of the physician as an individual and as a member of a profession.

A Psychology of Growth. By Bert I. Beverly, M.D., Rush Assistant Professor of Pediatrics, College of Medicine, University of Illinois, Chicago. Cloth. Price, $2.50. Pp. 235. McGraw-Hill Book Co., Inc., 330 W. 42d St., New York 18, 1947.

This book attempts to present the psychology of growth and development in a way which will help nurses to gain an insight into their own problems as well as those of their patients. It traces human growth and development from infancy, through childhood and adolescence to maturity. The first six chapters deal with the foundations of mental health, the 2 year old, adjusting to environment, intelligence, mental deficiency and the school child. In the remaining portions of the book fears, behavior problems and their causes, preadolescence, adolescence, juvenile delinquency and adult adjustment are discussed. A rather complete list of visual aids is included to supplement the material in the text. References for additional study are provided at the end of each chapter. The author uses a very practical approach to solving problems that may be encountered at various age levels. Numerous examples serve to illustrate methods of meeting individual needs at various stages of growth and development. Throughout the discussion stress is laid on the interdependence of mental, emotional and physical aspects of personality development. The book is clearly written and well printed. While it is not illustrated, the potentialities for correlation with the suggested visual aids offer many possibilities. It will probably have its greatest usefulness as a textbook for courses in psychology and in professional adjustment and as a reference work for the graduate nurse working in the field of pediatrics, psychiatry or public health. However, it may be read with profit by social workers, teachers and parents.

Complete Handbook on State Medicine. By J. Weston Walch. Paper. Price, $1.25. Pp. 178. J. Weston Walch, Box 66, Pearl St. Station, Portland, Maine, 1946.

This brochure is primarily for students preparing material for debate on the subject of "sickness insurance." It represents a new approach in debate manuals or at least a composite of most of the usual approaches. In an effort, a rather successful effort, to make the debate question interesting to the readers the author presents his material in a casual manner. One example is the title of chapter 1. "Ho, Hum, What's the Argument All About?" Another is his introduction to the Wagner bill. "A cat, they tell me, has nine lives, though you can't prove it by me. But this I do know—the Wagner-Murray-Dingell bill has had three." Throughout this informal presentation there is a great deal of factual data. Numerous references are made to well chosen sources for additional material. In the first thirty-two pages Mr. Walch explains the debate question and the terminology, discusses briefly the present systems of medical care and gives suggestions for preparing the debate. Much of the remainder of the publication is devoted to the preparation of both affirmative and negative briefs with supporting evidence, and references accompanying each brief. The final few pages contain suggestions for rebuttal. In presenting the supporting evidence the author has sacrificed completeness in order to use as many quotations as possible. Three hundred and forty-seven quotations appear for the affirmative and three hundred and forty-four are used in support of the negative. Too often they are one sentence statements plucked from some one's talk or article which, if read as a part of the whole, might mean something different than intended. Aside from this criticism, the publication is well done and should be in the hands of every debater.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

"PAINLESS" CORONARY OCCLUSION

To the Editor:—One wonders how many persons suffer "silent" coronary infarction. By that one means coronary thrombosis and infarction in which symptoms are absent, so slight or so atypical that the heart is not suspected or at least a definite diagnosis of coronary disease is not made. This question could be answered knowing how often scars of old infarcts are found in hearts of those in whom coronary thrombosis was never diagnosed during life. Such figures are probably available in many reports by pathologists, but I am unable to find any such report listed in the indexes. I would appreciate information on the subject.

D'Arcy Prendergast, M.D., Toronto.

ANSWER.—Painless or silent myocardial infarction due to coronary occlusion does exist, but its exact frequency has not yet been established. At times its occurrence has certainly been overestimated as the result of inadequate history taking. Most experienced observers who have seen hundreds of cases of acute myocardial infarction find that painless or silent acute coronary occlusion is distinctly uncommon. It may occur in the presence of severe shock and possibly severe acute alcoholism and quite possibly, but infrequently, in extremely insensitive persons. Its occurrence otherwise must be open to question. Two cases reported not long ago from Seattle (King, R. L., and Cleveland, F. E.: Acute Coronary Occlusion Without Pain, *Clinics of the Virginia Mason Hospital* 26:35, 1946) occurred in diabetic patients; the first patient was intermittently unconscious and the second patient was quite drowsy, doubtless affected by an inadequately controlled diabetic state.

A recent review of 78 cases of myocardial infarction at the Massachusetts General Hospital in which necropsy was performed gave no history of pain in 9, with serious shock or coma or cerebral vascular accident present in 10 others in which pain could not be inquired about.

VESICAL AND PROSTATIC CANCER

To the Editor:—In the Jan. 25, 1947 issue of The Journal on page 279 vesical and prostatic carcinoma is discussed. The following questions relate to that subject: 1. When the spread is along the ejaculatory ducts what are the early and late symptoms besides being able to palpate the growth in the prostatic urethra? 2. What would be the difference in the early and late symptoms when the metastases occur along the vertebral system of veins instead of along the ejaculatory ducts? 3. What is meant by the term "median bar" of the prostate? Is it prone to become more cancerous than any other portion of the prostate and if the median bar is somewhat enlarged is it as likely to be benign as to be malignant? 4. In a transurethral resection of the prostate is the ejaculatory function of the ejaculatory duct permanently lost? 5. Babcock's Surgery speaks of an early cystitis. Once cystitis is established I take it that the condition is intractable and remains a symptom in spite of any and all treatment medically. Is this true? 6. Is the prostate considered one of the genital organs?

M.D., Kansas.

ANSWER.—1. The spreading of carcinoma along the ejaculatory ducts could indicate its origin in the posterior lobe. Cancer of the posterior lobe is manifested by induration and obliteration of the median prostatic groove proximal to the veramontanum. Early symptoms of carcinoma of the prostate may be absent. Extension along the ejaculatory ducts may easily produce unexplained distention of the seminal vesicles. Carcinoma may be suspected early when the prostate is palpated over an instrument and a nodule is present.

2. Early symptoms of metastases by way of the vertebral system of veins may be limited to localized pain. Early x-rays of the spinal column will be negative. Later osteoclastic bone changes will confirm the suspicion of metastases.

3. A median bar implies hypertrophy of the posterior commissure of the prostate. A median bar is not apt to become cancerous; the enlargement is usually benign and consists of fibrous or adenomatous tissue.

4. The function of the ejaculatory duct following transurethral surgery is not lost unless it is inadvertently removed.

5. Hunner's ulcer or interstitial cystitis with a contracted bladder has been referred to as an intractable cystitis. Cystitis is usually amenable to treatment, particularly when the cause can be eradicated.

6. The prostate is a male sex organ and is a link in the male genital system.

DISPOSAL OF SEWAGE AND WATER BORNE DISEASE

To the Editor:—I should like your opinion on the following two statements:

1. It has been estimated that 70 per cent of sewage in the United States is dumped into surface waters without treatment.

2. In spite of the health hazards involved, the practice has been continued because of the cost of treating sewage.

Is the A. M. A. cognizant of this practice? Is there a greater prevalence of water borne diseases in those areas of the United States where sewage is dumped into surface waters without treatment? If so, should not the public be enlightened with regard to this practice with the hope that it would insist on effective sewage control systems regardless of cost?

David J. Sandusky, M.D., Detroit.

ANSWER.—1. The sewage of somewhat more than 50 per cent of the total urban population of the United States is now treated, either by what is known as partial treatment or by complete treatment.

2. The practice of discharging raw sewage has been continued not only because of the cost involved but because of a variety of complex legal, administrative and fiscal issues. Cost is a significant item in these considerations, but not the only item. Progress in correcting this situation has been materially retarded during the war period and, in the present high level costs of labor and materials, in the postwar period.

Administrative attack on the problem, however, continues at a high level and it may be anticipated that the next ten years will see billions of dollars expended in correcting the situations to which you refer.

The American Medical Association is cognizant of the practice and is lending its efforts toward increasing the rate of correction. Water borne diseases in general in the United States are now at their lowest point in our history, as the result obviously of the combined efforts of engineering and medical officials over the last half century.

SENILE OSTEOPOROSIS OR HYPERPARATHYROIDISM

To the Editor:—A woman aged 57 injured her back three years ago and since that time has had constant back pain and progressive kyphosis. X-rays of the skull and lumbar spine showed loss of normal bone density. The tables of the skull were mildly granular, suggesting the possibility of low grade hyperparathyroidism. Blood calcium was 10 mg. per hundred cubic centimeters, inorganic phosphorus 2.8 mg. per hundred cubic centimeters and serum alkaline phosphatase 46.3 Bodansky units. Is this the picture of senile osteoporosis or hyperparathyroidism? How may I further establish the diagnosis?

John Shelton Reed, M.D., Kingsport, Tenn.

ANSWER.—The high serum alkaline phosphatase level is against senile osteoporosis. Furthermore, one seldom sees demineralization of the skull in that condition. The normal serum calcium level is against hyperparathyroidism unless the patient had at the same time a low serum protein level. The blood findings are consistent with osteomalacia.

To establish a diagnosis, one would like repeat serum calcium, phosphorus, phosphatase determinations, a serum protein determination with albumin/globulin ratio if possible, and a quantitative twenty-four hour urine estimation for calcium. A low serum calcium excretion would be strong evidence against hyperparathyroidism, moderate evidence against osteoporosis and strong evidence in favor of osteomalacia. A high urinary calcium excretion would not rule out osteomalacia, however.

COSMETIC EFFECT AFTER REMOVAL OF FACIAL CYST

To the Editor:—Has any satisfactory method been developed for removal of a sebaceous cyst from the skin without leaving a scar or other disfigurement? The patient is a society woman aged of 10 who has a sebaceous cyst about the size of a lima bean in the skin of the cheek. This was recently infected, red and tender but is now quiescent and painless. My previous experience has been that excision is always followed by some scarring, which it is hoped to avoid in this case. At present the nodule is not too unsightly, but it seems to cause her a great deal of concern.

Willis P. Baker, M.D., Santa Ana, Calif.

ANSWER.—There is no possible way to remove a cyst of this type without an incision through the skin. The best cosmetic result can be obtained if the line of incision is placed so that it will parallel a normal skin fold or wrinkle. The size of the incision should be made as small as will permit legitimate exposure of the tumor. Minimal postoperative scarring can be obtained if the wound edges are sutured with small interrupted stitches of fine nonabsorbable suture material. The stitches should be removed within three days so as to avoid potential stitch hole scarring, but the wound edges should be supported with some material such as a dumb-bell strip of adhesive for two to three weeks postoperatively. Failure to carry out the latter step may permit the fresh scar to widen from underlying muscle activity.

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CELLOSOLVE ACETATE

To the Editor:—I should like information as to the possible toxic effects of the fumes of Cellosolve Acetate (ethylene glycol monoethyl ether monoacetate) derives from animal experiment rather than from human beings actually exposed in industry. The vapor pressure of Cellosolve Acetate at 20 C. is 1.25 mm. of mercury, which is low. Obviously vapor pressure at 60 C. will be higher. According to Von Oettingen and Jirouch (*J. Pharmacol. & Exper. Therap.* 42:355 [Aug.] 1931) it hemolyzes blood in vitro and causes the formation of methemoglobin. It has a distinct depressant effect on the central nervous system and causes, first, irritation and then depression of the sensory nerve endings and paralysis of the motor nerve fibers. It depresses the perfused frog heart and organs with smooth muscle structure. It causes distinct irritation of the conjunctiva of the rabbit's eye, characterized by hyperemia and edema of the lower eyelid. There are no reports with regard to the toxic action in man, but the data mentioned appear to indicate that it is by no means a harmless material. Hamilton and Johnstone (New York, Oxford University Press, 1945) in referring to the work just cited note that repeated exposures of rats to vapors of glycol ethers, 300 to 400 parts per million, show that "small but measurable effects" on the cellular elements of the blood appear, such as increase in young granulocytes and decrease in hemoglobin concentration and red cell count.

Browning (British Research Medical Council Report number 80, 1937) places the toxicity level as that of Cellosolve (ethylene glycol monoethyl ether). The toxicity of the latter is well established and is revised by Browning. Still further information derives from the work of Smyth and others (*J. Indust. & Toxicol.* 28:259, 1941). This group determined the MLD/50 on small animals for some sixty glycols and related compounds. Cellosolve Acetate proves to stand about midway in the group. The vapors of Cellosolve Acetate may lead to eye irritation and may influence taste and odor perception. Higher concentration may serve as a central nerve depressant and may act adversely on the renal system. Deviation from the usual in the blood picture may constitute a prime warning of damage. It is unlikely that this substance will exert any direct influence on sexual capacity.

ADMINISTRATION OF HISTAMINE IN PRESENCE OF CORONARY DISEASE

To the Editor:—In recent months there has appeared in the lay press some reference to the use of histamine in the treatment of particular vascular complaints of diagnosis that is otherwise uncomplicated. I have under my care such a person but who has had in recent years two episodes of coronary artery disease, and I have hesitated to give this histamine in an effort to overcome these attacks of dizziness because of the fact that I was afraid there might be some danger associated with it.

Oliver L. Shaw, M.D., Greensboro, N. C.

ANSWER.—In the heart-lung preparation of human beings, histamine dilates the coronary arteries. Presumably the same action occurs in the living subject.

Patients with Ménière's disease and coronary heart disease have been given a 1:250,000 dilution of histamine administered intravenously without producing untoward symptoms. The rate of administration should be carefully regulated.

Peters and Horton recently published a report on 25 normal subjects in whom continuous intravenous administration of histamine was given at rates varying from 0.0017 to 0.044 mg. per minute. Significant changes were observed in the electrocardiograms in 24 of the 25, but the effects were considered to be of minor physiologic importance. The most common change was the loss of amplitude of the T waves in different leads, sometimes in all leads, which, in some cases, proceeded to either the isoelectric level or to inversion of the wave. The extent of loss of T wave voltage was roughly and directly parallel to the rate of administration of histamine. In some cases, however, the effect of histamine was lost, and the T waves recovered either partially or completely their former amplitude in spite of a continued and sometimes increased dosage of histamine. The effect of histamine on the T waves disappeared within five to fifteen minutes after injection of the drug was discontinued.

The action of histamine on coronary circulation varies in different species. Essex and his colleagues found that histamine increased the coronary flow in the unanesthetized dog.

POSTRADIATION TREATMENT OF CARCINOMA OF CERVIX

To the Editor:—A woman aged 48, who weight 80 pounds (36 Kg.), has a grade 1 carcinoma and carcinoma of the cervix apparently early and confined to the cervix. Six months ago she was treated with 5,400 mg. hours of radium and 4,500 roentgens of x-rays, half value layer 1.5. There is no evidence of recurrence of cancer. The cervix has healed. Is total hysterectomy advised at the present time?

G. B. Hubbard, M.D., Jackson, Tenn.

ANSWER.—Although the cervix may appear to be entirely healed, Martzloff has shown that viable tumor cells may remain entrapped within the cervix and cause recurrence at a later date. The patient described in the query, because of age, weight and an apparently early lesion, is an ideal subject for the radical hysterectomy of the Wertheim type. Therefore one could not disagree with those who would favor removal of the uterus by this procedure. However, the high survival rate (80 per cent) of patients with such early lesions treated with radium and x-rays in adequate dosage, such as has been given this patient, justifies watchful expectancy, postponing surgical removal until definite evidence of recurrence can be demonstrated.

INFECTIONS AMONG PATHOLOGISTS AND MORTICIANS: WEARING OF RUBBER GLOVES

To the Editor:—Are there any statistics available showing the incidence of infection which morticians and pathologists have contracted from working on corpses? It is assumed that diseased changes set in shortly after death and that organisms are not viable long. However, there are questions often in gentlemen's minds. Should there be a question in their mind as to the source of such infections, not only of tuberculosis but of other infections. A coroner contends that the position of using gloves in examining bodies is the wrong position, as the prick of a glove and finger makes for optimum conditions of culture medium, thus reviving the organisms sufficiently to be viable and pathogenic and making it possible to transmit infection to the examiner. This has caused some controversy in a mortician's organization. Any information you can give on this matter will be of help and interest.

J. A. Cramer, M.D., Denver.

ANSWER.—Statistics showing the incidence of infection (including tuberculosis) which morticians and pathologists have sustained from working on corpses have not been found. There are isolated cases of tuberculosis among embalmers. Some believe their infections traceable to given instances. Similarly, instances are known wherein embalmers and pathologists respectively have acquired infection as the result of an accidental wound during embalming procedure or while conducting a postmortem examination.

In supporting the hazardous concept of the embalmer's occupation, insurance classifications offer a clue. The majority of companies who write health and accident policies regard men in this occupation as class C and D risks.

Several years ago the question concerning the value of rubber gloves as a safety measure was raised in another mortician's organization. Again statistics were not available for supporting either point of view. Nevertheless an opinion given by an eminent pathologist was to the effect that there could be little question that pathologists suffered many more hand infections than physicians in general. He always wore gloves. He believed that organisms which would produce an infection of the hand are deposited within the skin when the finger is pricked and that they are uninfluenced by warmth and moisture of the hand and glove.

Between 1932 and 1935 at the Los Angeles County General Hospital there was a difference of opinion among the classes, particularly between those who had worked around a funeral home before enrolling in school, as to the merit of rubber gloves. However, every student was required to wear them while in the preparation room. The importance of caring for gloves properly while in use and in cleansing them for subsequent use was stressed. During this interval approximately two hundred students received their practical training in preparing all types of cases. Only one instance of infection was reported. It was not due to accident while wearing rubber gloves.

There is sufficient periodic interest in this subject to justify a bona fide investigation to settle this long controversy.

MENSTRUATION AND BATHING

To the Editor:—Aside from the esthetic factors, is menstruation a contraindication for bathing, particularly in cold water, or swimming?

M.D., Iowa.

ANSWER.—Menstruation is not a contraindication to any form of bathing except when the flow is profuse. In such cases a hot tub bath might increase the loss of blood still further.

OPEN VERSUS CLOSED TREATMENT OF FRACTURES

To the Editor:—Has it ever been definitely proved that simple fractures treated by open reduction heal more slowly than simple fractures treated by closed methods, comparing, of course, fractures of the same site, degree of severity and patients of similar age groups? That fractures treated by open operation heal more slowly has seemed to me to be quite evident, but there are so many variable factors it is difficult to prove the point.

Herbert J. Ferrari, Lieutenant, M. C., U. S. Army.

ANSWER.—The point has not been definitely proved but is suspected by some experienced surgeons and laughed at by others. Advocates of the open method often disclaim slower healing and claim on the contrary more rapid repair, saying that perfect reduction, supposedly obtained by operation, calls for less effort on the part of the patient to form callus. This is because the perfect approximation of fragments requires a smaller amount of new bone formation, there are smaller gaps to bridge and the various bone elements are closely apposed. They also may claim that shorter immobilization is required and earlier use of the part is permitted to restore muscle volume and increased blood supply in the area. Many catastrophes have resulted from loose and unskilful application of this so-called principle because it provides a too short immobilization and defeats the process of healing itself by permitting too early and too great strain at the fracture site.

The most difficult factor to weigh is the bone forming power of any single person even in the same age group. There may also be a minimal degree of totally unrecognized infection. One still unmeasured factor is the loss at (early) operation of much if not all of the extravasated blood and exudate around the fracture site, amounting in major fractures to several ounces, which runs out as soon as the fracture is cut down on. This contains not only calcium and phosphates but also phosphatase useful in the healing process and probably has much to do with sustaining a favorable p_H in the early part of the repair.

No line of treatment seems to hasten the normal process of final complete calcification of callus after closed fracture in healthy persons, but many factors such as nonexpert operating, too short immobilization or unwise weight bearing or use may prolong it. This does not apply to greatly delayed union or nonunion.

TREATMENT OF CARBON MONOXIDE COMA

To the Editor:—Which are the therapeutic measures at present adopted in the United States in cases of coma from carbon monoxide? Are the blood transfusions still used?

Jean Sedoril, M.D., Brussells, Belgium.

ANSWER.—In cases of coma due to carbon monoxide poisoning it is important to supply 100 per cent oxygen or 7 per cent carbogen (7 per cent CO_2+ 93 per cent O_2) as quickly as possible to support the heart and to remove the carbon monoxide from the blood. It has been found that as far as immediate survival and neurologic sequels are concerned it matters not which of the two gases is used. In either case (which is also true if air is used) it is important to keep the minute volume of pulmonary ventilation as high as possible without harming the lungs for a period of five to fifteen minutes. By the end of this time the carbon monoxide saturation of the blood has been reduced to safe limits (5 to 10 per cent) and if the patient is still in coma blood transfusion will not be of assistance unless the patient is in a state of circulatory shock. Blood transfusion has no place in the treatment of carbon monoxide asphyxia in the absence of circulatory shock. Coma may sometimes persist for two or three hours after the oxygen saturation of the blood has returned to 90 per cent in the presence of a normal blood pressure, following which full functional recovery may result; the cause of this coma is uncertain. The prognosis is grave as regards neurologic sequels if the coma persists longer than thirty minutes after the reduction of the oxygen saturation of the blood to 90 per cent.

SULFHYDRYL FOR ROENTGEN RAY BURNS

To the Editor:—Is sulfhydryl of value in the treatment of chronic x-ray burns of the hands? (Goodhue, A. L.: Importance of Sulfhydryl in Treatment of Corneal and X-Ray Burns, Am. J. Surg. 73:108 [Oct.] 1946; abstr. The Journal, Jan. 11, 1947, p. 131.) Is penicillin sulfhydryl sprayed on ulcers or is penicillin used in 1:1 spray? What strength penicillin is used and how is it mixed?

Robert H. Kerr, M.D., Alma, Neb.

ANSWER.—The article to which reference is made in the query is the only report available on treatment by sulfhydryl of lesions produced by roentgen rays. Until further reports are available the treatment must be considered experimental, but apparently it is quite harmless. It appears from the original article that when penicillin is used it is applied in solution separately from the sulfhydryl spray and ointment.

TOXIC ADENOMA OF THYROID AND PROPYL-THIOURACIL

To the Editor:—A patient with a toxic adenoma of the thyroid gland developed a successful reaction on taking thiouracil in doses as low as 25 mg. daily. Is there any other related compound that may be used in place of thiouracil? If there is, please give me the dosage and untoward effects.

Mavis I. Gerner, M.D., Chester, N. Y.

ANSWER.—One could try propyl-thiouracil. This is begun with a dose of 50 mg. three times a day. It is sometimes necessary to give as much as 200 or 300 mg. daily to produce the maximum effect. It should, however, be borne in mind that response to this drug may be rather slow, particularly by a patient with toxic adenoma. The reactions produced by propyl-thiouracil are approximately those produced by thiouracil except that they occur less frequently.

The most serious complication is the development of leukopenia and agranulocytosis, and patients receiving the drug should be observed with great care. A white blood cell count and a differential count should be made at frequent intervals.

There is some difference of opinion as to whether the drug should be used for the medical management of patients with toxic adenoma. It is probably fair to say that the majority of observers favor using it for preoperative preparation in this condition. However, there is no doubt that in many patients with toxic adenoma the condition can be controlled completely with medical measures alone.

SPLENIC ANEMIA AND PREGNANCY

To the Editor:—A woman aged 27 is three months pregnant. This is her third pregnancy. The patient's first child died at three months of splenic anemia and "enlarged liver." In the patient's second pregnancy labor was induced at eight months and the child lived for five weeks, probably dying of pneumonia. My patient has splenic anemia. The patient's father died of splenic anemia. The patient has had two series of x-ray treatments and two transfusions; she has been taking daily liver injections for four years; also she is getting folic acid 5 mg. three times a day. She is anxious to permit pregnancy to go to term and will take transfusions as indicated, also other therapy. Should pregnancy be permitted to continue? If so, what should the course be?

M.D., Asheville, N. C.

ANSWER.—In the absence of data concerning the blood picture it is difficult to suggest the proper therapy for the anemia. It is assumed that the patient's blood is now normal from the daily injections of liver extract for four years and the folic acid. Ordinarily it would be wise to allow the pregnancy to continue unless the anemia becomes extremely severe and cannot be controlled by transfusions, or the size of the spleen limits the space in the abdomen to such an extent that with the enlarged uterus the discomfort is too great. It may be well to investigate the Rh factor in the blood of the patient and her husband before more transfusions are given, as she may be Rh negative and have developed anti-Rh substance from the previous transfusions (if they were Rh+).

SKIN STAINING FROM FRUIT JUICES

To the Editor:—I am seeing a few patients who work in a fruit preserve factory. From contact with fruit juice, their hands become stained dark. Is there any way to prevent or decrease this staining?

Albert Abraham, M.D., Morristown, N. J.

ANSWER.—The wearing of rubber gloves with impervious sleeves fastened over the glove at the wrist will prevent the fruits or their juices from touching the skin.

Washing the stained hands after work in a 1:2,000 solution of potassium permanganate followed by washing in a 1 per cent solution of sodium sulfite to remove the permanganate stain will bleach the stains. After this procedure the hands should be washed in soap and water and dried, and an emollient cream such as equal parts of lanolin and cold cream should be rubbed into the skin.

MANNITOL HEXANITRATE

To the Editor:—In The Journal, April 5, 1947, page 1042, a query discusses mannitol hexanitrate for hypertension. I believe that the statement given in the answer is not in accordance with generally accepted views with regard to the action of compounds of this type. In the answer the statement is made that the nitrite ion is extraordinarily unstable. This is not in accordance with fact. Also the statement is made that the concentration of nitrite ion in the blood is in the order of magnitude of 1 microgram per hundred cubic centimeters. This has been found to be incorrect often. Further, it is stated that why some of the compounds are more active than others is not well understood. The mechanism of the action of organic nitrates and inorganic nitrites in hypertension has been recently elucidated.

John C. Krantz Jr., Baltimore,
Professor of Pharmacology, University of Maryland.